U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

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Search Site

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Type f Search

_____ N.A. Sequence

_____ A.A. Sequence

_____ Structure

_____ Bibliographic

Vendors

_____ IG Suite

_____ STN

_____ Dialog

_____ APS

_____ Geninfo

_____ SDC

_____ DARC/Questel

_____ Other

Fisher, T.
10/015184

(FILE 'REGISTRY' ENTERED AT 11:16:08 ON 03 APR 2003)
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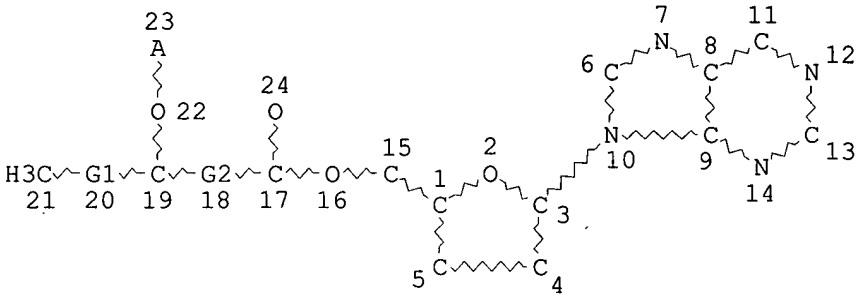

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REP G2=(0-5) CH2
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
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SEARCH TIME: 00.00.01

FILE 'HCAPLUS' ENTERED AT 11:20:19 ON 03 APR 2003
L6 11 S L5

L6 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:529169 HCAPLUS
DOCUMENT NUMBER: 131:170633
TITLE: Preparation of amino acid-containing prodrugs
INVENTOR(S): Johansson, Nils Gunnar; Zhou, Xiao-xiong; Wahling, Horst; Sund, Christian; Wallberg, Hans; Salvador, Lourdes; Lindstrom, Stefan
PATENT ASSIGNEE(S): Medivir AB, Swed.
SOURCE: PCT Int. Appl., 167 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9941275	A1	19990819	WO 1999-SE194	19990215

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WO 9909031 A1 19990225 WO 1998-SE1467 19980414
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ZA 9807267 A 19990215 ZA 1998-7267 19980813

EP 1123935 A2 20010816 EP 2001-103370 19980814

EP 1123935 A3 20010905
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NZ 508502 A 20020426 NZ 1998-508502 19980814

ZA 9901148 A 19990812 ZA 1999-1148 19990212

CA 2318978 AA 19990819 CA 1999-2318978 19990215

AU 9932820 A1 19990830 AU 1999-32820 19990215

AU 754733 B2 20021121

EP 1054891 A1 20001129 EP 1999-932500 19990215
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CA 2325523 AA 19991014 CA 1999-2325523 19990330

WO 9951613 A1 19991014 WO 1999-SE528 19990330
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EP 1121366 A1 20010808 EP 1999-921327 19990330
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WO 2000047561 A1 20000817 WO 1999-SE1403 19990818
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AU 9956658 A1 20000829 AU 1999-56658 19990818

EP 1150956 A1 20011107 EP 1999-943591 19990818
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JP 2002536435 T2 20021029 JP 2000-598482 19990818

US 2002128301 A1 20020912 US 2001-927254 20010810

PRIORITY APPLN. INFO.:

SE 1998-452	A	19980213
SE 1998-469	A	19980216
SE 1998-1216	A	19980403
WO 1998-SE1467	W	19980414
ZA 1998-7267	A	19980813
SE 1998-3438	A	19981007
SE 1997-2957	A	19970815
SE 1997-4147	A	19971112
EP 1998-939041	A3	19980814
NZ 1998-502837	A1	19980814
US 1999-249317	A	19990212
WO 1999-SE194	W	19990215
WO 1999-SE528	W	19990330
WO 1999-SE1403	W	19990818

OTHER SOURCE(S): MARPAT 131:170633

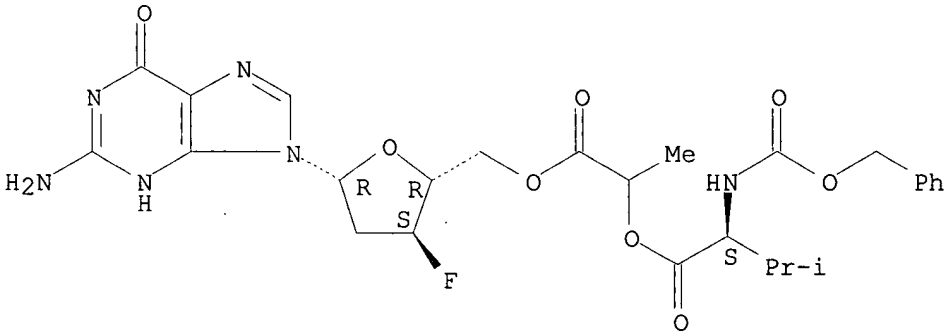
AB Pharmaceutical compds. or intermediates in their synthesis D*-Linker*(R2')k-R2 [R2 and R2' (if present) is the amide or ester residue of an aliph. amino acid, k is 0 or 1, D* is a drug residue bearing an accessible function selected from amine, hydroxy and carboxy, or a group amenable to attachment to the accessible function, Linker* is an at least bifunctional linker comprising a first function bound to the accessible function spaced from a second function forming an amide or acyl bond with the aliph. amino acid] were prepd. Thus, 2',3'-dideoxy-3'-fluoro-5'-O-{3-[1,3-bis(L-valyloxy)-2-propyloxycarbonyl]propanoyl}guanosine was prepd. and shown to provide significantly enhanced oral bioavailability relative to the active metabolite 2',3'-dideoxy-3'-fluoroguanosine.

IT **220750-76-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of amino acid-contg. prodrugs)

RN 220750-76-5 HCAPLUS

CN L-Valine, N-[(phenylmethoxy)carbonyl]-, monoester with 2',3'-dideoxy-3'-fluoroguanosine 5'-(2-hydroxypropanoate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **238400-75-4P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid-contg. prodrugs)

RN 238400-75-4 HCAPLUS

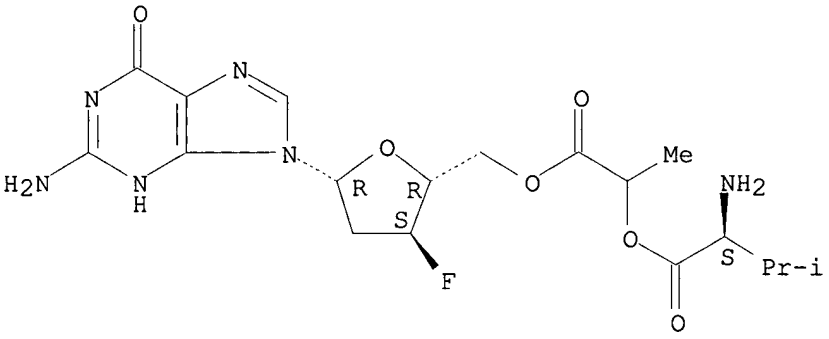
CN L-Valine, ester with 2',3'-dideoxy-3'-fluoroguanosine

5'-(2-hydroxypropanoate), monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 220750-46-9
CMF C18 H25 F N6 O6

Absolute stereochemistry.



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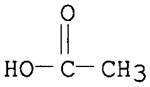
CMF C2 H4 O2



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:139847 HCAPLUS
DOCUMENT NUMBER: 130:209924
TITLE: Preparation of amino acid-containing nucleoside esters as inhibitors of retroviral reverse transcriptase and hepatitis B virus DNA polymerase
INVENTOR(S): Zhou, Xiao-Xiong; Johansson, Nils-Gunnar; Wahling, Horst
PATENT ASSIGNEE(S): Medivir AB, Swed.
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO	9909031	A1	19990225	WO 1998-SE1467	19980414
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AU	728892	B2	20010118		
EP	988304	A1	20000329	EP 1998-939041	19980814
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ZA	9901148	A	19990812	ZA 1999-1148	19990212
CA	2318975	AA	19990819	CA 1999-2318975	19990212
WO	9941268	A1	19990819	WO 1999-SE189	19990212
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US	6458772	B1	20021001	US 1999-249317	19990212
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WO	9941275	A1	19990819	WO 1999-SE194	19990215
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JP	2002503673	T2	20020205	JP 2000-531466	19990215
CA	2325523	AA	19991014	CA 1999-2325523	19990330
WO	9951613	A1	19991014	WO 1999-SE528	19990330

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EP 1121366	A1	20010808	EP 1999-921327	19990330
JP 2002510698	T2	20020409	JP 2000-542334	19990330
AU 9932819	A1	19990830	AU 1999-32819	19990830
AU 732408	B2	20010426		
US 2002128301	A1	20020912	US 2001-927254	20010810

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PRIORITY APPLN. INFO.:

SE 1997-2957	A	19970815
SE 1997-4147	A	19971112
SE 1998-452	A	19980213
SE 1998-469	A	19980216
SE 1998-1216	A	19980403
WO 1998-SE1467	W	19980414
ZA 1998-7267	A	19980813
EP 1998-939041	A3	19980814
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SE 1998-3438	A	19981007
US 1999-249317	A	19990212
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WO 1999-SE528	W	19990330
WO 1999-SE1403	A2	19990818

OTHER SOURCE(S): MARPAT 130:209924

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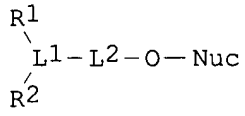

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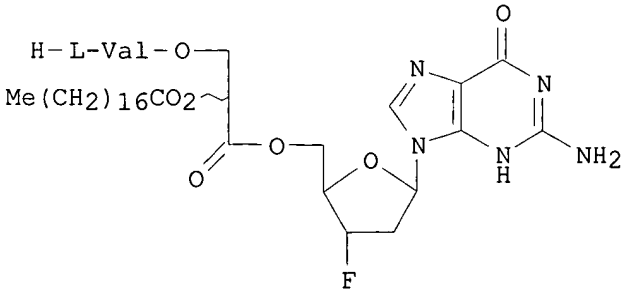


II

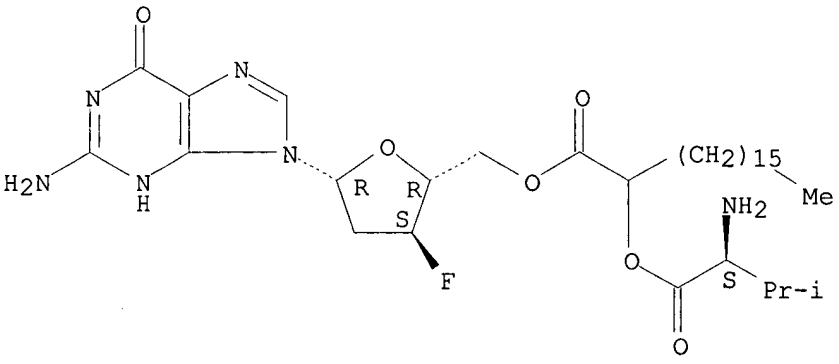
AB Nucleoside analogs I [Nuc = nucleoside analog residue bonded through its single hydroxy group on the cyclic or acyclic saccharide moiety; R1 = optionally esterified or amide bonded OH, NH2, CO2H, C4-C22

satd. or unsatd., optionally substituted fatty acid or alc., aliph. L-amino acid; R2 = aliph. L-amino acid residue; L1 = trifunctional linker group; L2 = bond, difunctional linker group] and pharmaceutically acceptable salts thereof have favorable pharmacol. properties and are antivirally active. Thus, nucleoside ester II was prepd. by esterification of 2',3'-dideoxy-3'-fluoroguanosine (FLG) with 3-(N-benzyloxycarbonyl-L-valyloxy)-2-stearoyloxypropanoic acid followed by hydrogenolysis. II showed 81.5% bioavailability of FLG after 6 h in a rat bioavailability assay model.

IT **220750-41-4P 220750-46-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid-contg. nucleoside esters as inhibitors of retroviral reverse transcriptase and hepatitis B virus DNA polymerase)

RN 220750-41-4 HCAPLUS
CN L-Valine, monoester with 2',3'-dideoxy-3'-fluoroguanosine 5'-(2-hydroxyoctadecanoate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220750-46-9 HCAPLUS
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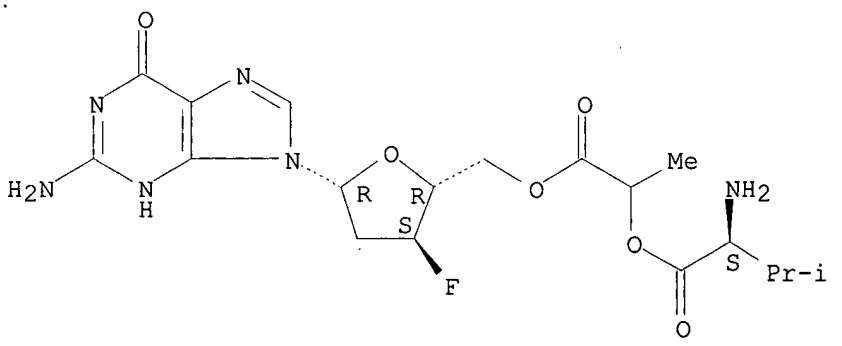
Absolute stereochemistry.

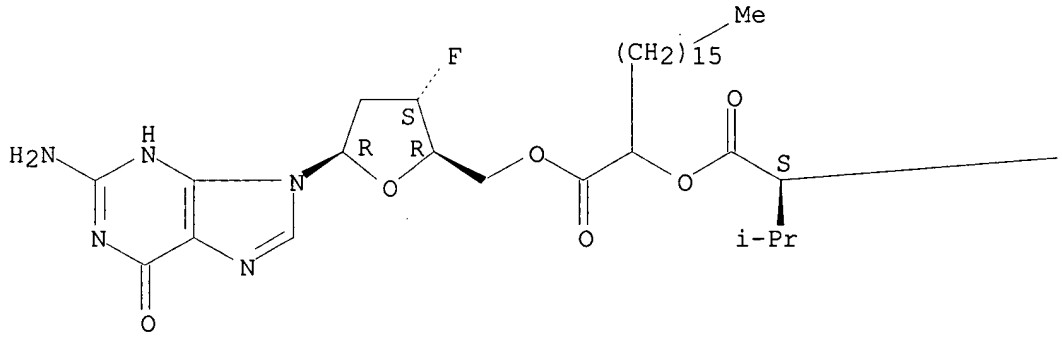


IT **220750-67-4P 220750-76-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of amino acid-contg. nucleoside esters as inhibitors of retroviral reverse transcriptase and hepatitis B virus DNA polymerase)

RN 220750-67-4 HCAPLUS
CN L-Valine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-, monoester with 2',3'-dideoxy-3'-fluoroguanosine 5'-(2-hydroxyoctadecanoate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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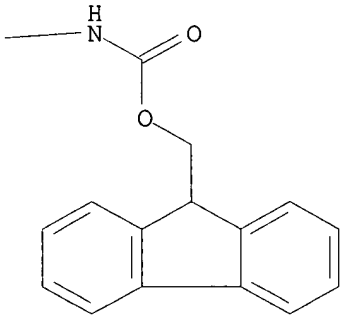
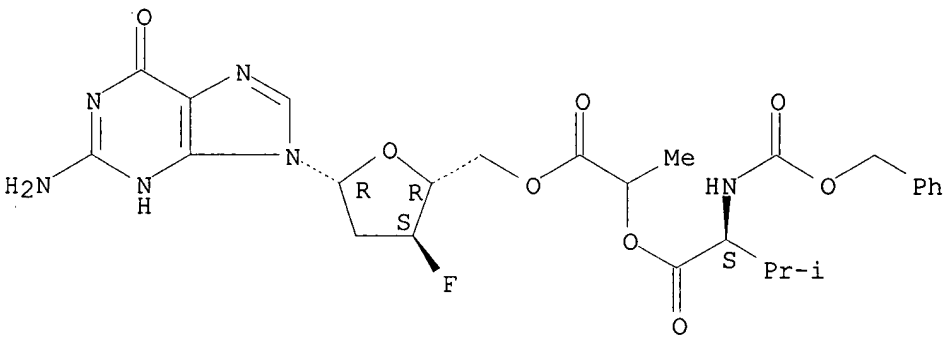


RN 220750-76-5 HCAPLUS
CN L-Valine, N-[(phenylmethoxy)carbonyl]-, monoester with 2',3'-dideoxy-3'-fluoroguanosine 5'-(2-hydroxypropanoate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

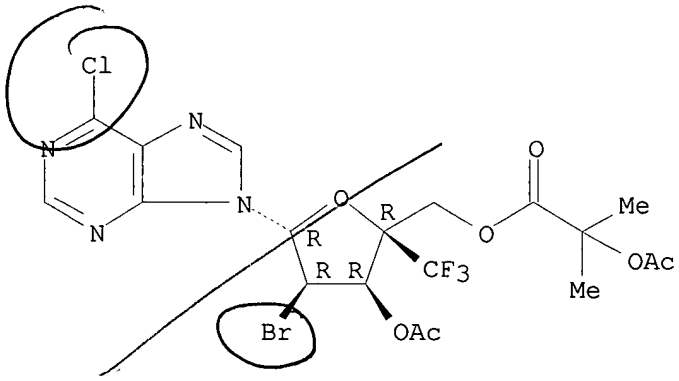
L6 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:784373 HCAPLUS
DOCUMENT NUMBER: 130:110528
TITLE: Synthesis of 4'-trifluoromethyl nucleoside analogs
AUTHOR(S): Kozak, Janusz; Johnson, Carl R.
CORPORATE SOURCE: Department of Chemistry, Wayne State University, Detroit, MI, 48202-3489, USA
SOURCE: Nucleosides & Nucleotides (1998), 17(12), 2221-2239
CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A strategy based on the use of (trifluoromethyl)trimethylsilane for introduction of the trifluoromethyl group at the C-4 of ribose has been developed and utilized in the synthesis of various novel 4'-trifluoromethylated nucleoside analogs. Screening of these analogs against HIV did not reveal significant biol. activity.

IT **219649-62-4P 219649-63-5P 219649-66-8P 219649-67-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of trifluoromethyl nucleoside analogs)

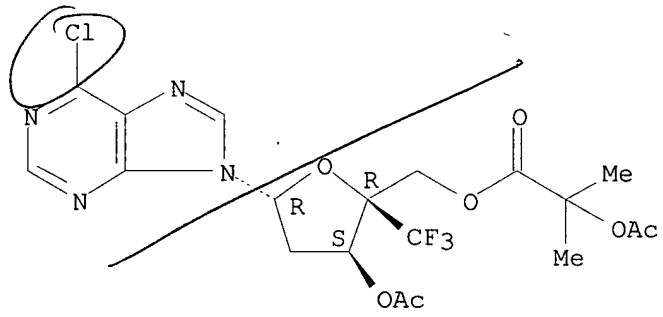
RN 219649-62-4 HCAPLUS
CN 9H-Purine, 9-[3-O-acetyl-5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-bromo-2-deoxy-4-C-(trifluoromethyl)-.beta.-D-ribofuranosyl]-6-chloro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



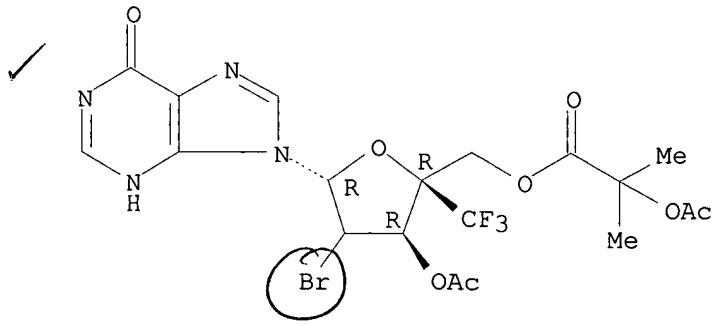
RN 219649-63-5 HCAPLUS
CN 9H-Purine, 9-[3-O-acetyl-5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-deoxy-4-C-(trifluoromethyl)-.beta.-D-erythro-pentofuranosyl]-6-chloro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



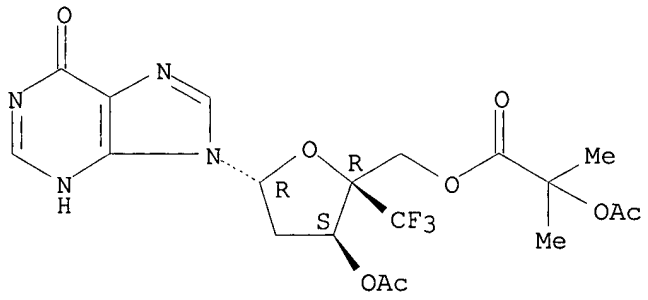
RN 219649-66-8 HCAPLUS
CN 6H-Purin-6-one, 9-[(2.xi.)-3-O-acetyl-5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-bromo-2-deoxy-4-C-(trifluoromethyl)-.beta.-D-erythro-pentofuranosyl]-1,9-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 219649-67-9 HCAPLUS
CN Inosine, 2'-deoxy-4'-C-(trifluoromethyl)-, 3'-acetate 5'-[2-(acetyloxy)-2-methylpropanoate] (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

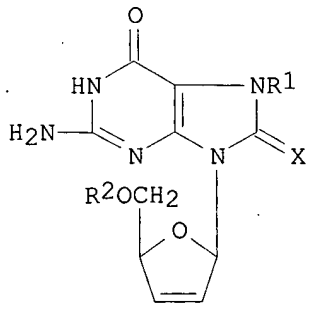


REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:795405 HCAPLUS
DOCUMENT NUMBER: 124:30279
TITLE: Preparation of 2'3'-dideoxy-2',3'-didehydro-7,8-disubstituted guanosines having immunostimulative effect
INVENTOR(S): Goodman, Michael G.; Chen, Robert; Reitz, Allen
PATENT ASSIGNEE(S): The Scripps Research Institute, USA
SOURCE: U.S., 10 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5441942	A	19950815	US 1994-250483	19940527

PRIORITY APPLN. INFO.: US 1994-250483 19940527
OTHER SOURCE(S): MARPAT 124:30279
GI



I

AB Immunostimulating 7,8-disubstituted guanine derivs. that also contain a .beta.-9,1'-linked-2',3'-dideoxy-2',3'-didehydroribosyl

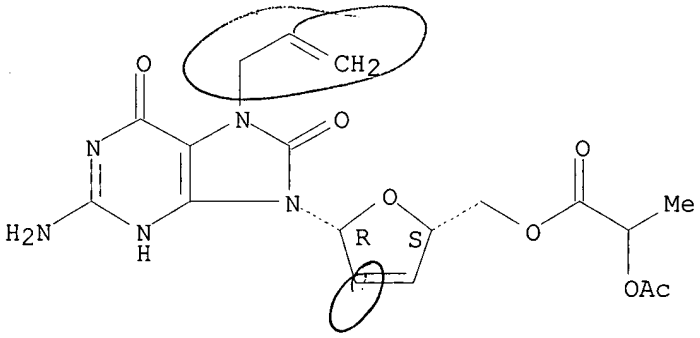
substituent [I; X = O, S; R1 = (un)substituted C1-7 hydrocarbyl; R2 = H, C1-8 acyl] and pharmaceutically acceptable base addn. salts thereof are prepd. Thus, a suspension of 5 g 7-allyl-8-oxoguanosine in MeCN was treated with 15.5 g 2-acetoxyisobutyryl bromide and the resulting mixt. was refluxed for 30 min to give, after workup and silica gel chromatog., a rust-colored solid of the expected mixt. of vicinal 2',3'-bromoacetates (90% yield). The latter solid was dissolved in 80 mL EtOH and treated with 9 g Zn dust and 0.5 mL AcOH at room temp. for 4 h, followed by adding addnl. 3 g Zn dust and heating the mixt. at 40.degree. for 40 h, to give, after workup, treatment with NaOMe in MeOH, and silica gel chromatog., 1.7 g 2',3'-dideoxy-2',3'-didehydroloxoribine, i.e. I (X = O, R1 = allyl, R2 = H) (II). II in vitro showed ED50 of 11-12 .mu.M for activating NK cells vs. 15-34 .mu.M for loxoribine.

IT **171604-13-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of dideoxydidehydroguanosine derivs. as immunostimulants)

RN 171604-13-0 HCAPLUS

CN Guanosine, 2',3'-didehydro-2',3'-dideoxy-7,8-dihydro-8-oxo-7-(2-propenyl)-, 5'-[2-(acetyloxy)propanoate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:64940 HCAPLUS

DOCUMENT NUMBER: 123:9835

TITLE: Small-Molecule Immunostimulants. Synthesis and Activity of 7,8-Disubstituted Guanosines and Structurally Related Compounds

AUTHOR(S): Reitz, Allen B.; Goodman, Michael G.; Pope, Barbara L.; Argentieri, Dennis C.; Bell, Stanley C.; Burr, Levelle E.; Chourmouzis, Erika; Come, Jon; Goodman, Jacquelyn H.; et al.

CORPORATE SOURCE: Medicinal Chemistry Department, R. W. Johnson Pharmaceutical Research Institute, Spring House, PA, 19477, USA

SOURCE: Journal of Medicinal Chemistry (1994), 37(21), 3561-78
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of 7,8-disubstituted guanosine derivs. was designed and prepd. as potential B-cell-selective activators of the humoral

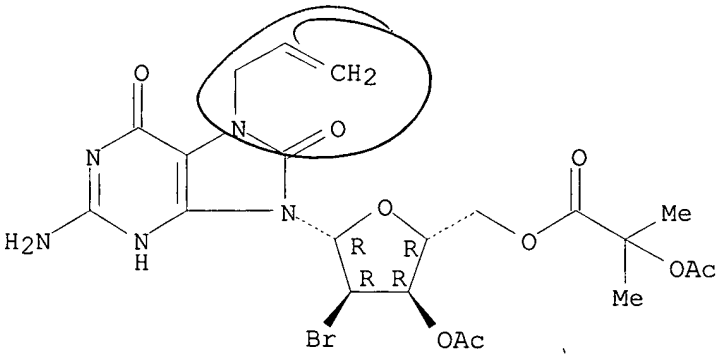
immune response. These compds. were evaluated for their ability to act as B-cell mitogens and to augment the antibody response of B cells to sheep red blood cell (SRBC) challenge (adjuvanticity). In addn., they were tested for their ability to stimulate the natural killer (NK) cell response in murine in vitro cell assays. Certain of the compds. demonstrated in vivo activity when administered either i.v., s.c., or orally. Compds. bearing hydroxyalkyl, aminoalkyl, or substituted aminoalkyl substituents on this 7-position were weakly active. Oxo, thioxo, and seleno groups on C-8 of the guanosine ring all imparted strong activity, whereas other larger substituents did not (e.g., N:CN). A total of 80 compds. were prepd. and evaluated for their immunostimulating activity. Within this group, compds. could be divided into those that were active in all three assays, those that displayed some measure of selectivity for the adjuvanticity assay, and those that preferentially activated NK responses. Because of its overall biol. profile and ease of synthesis,7-allyl-8-oxoguanosine (loxoribine, RWJ-21757) was chosen for further development. It is among the most potent compds. evaluated in the three biol. assays.

IT **163668-53-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and of immunostimulant activity of 7,8-disubstituted guanosines and structurally related compds.)

RN 163668-53-9 HCAPLUS

CN Guanosine, 2'-bromo-2'-deoxy-7,8-dihydro-8-oxo-7-(2-propenyl)-, 3'-acetate 5'-[2-(acetyloxy)-2-methylpropanoate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:	1993:626349 HCAPLUS
DOCUMENT NUMBER:	119:226349
TITLE:	Preparation of deoxynucleoside derivatives
INVENTOR(S):	Serafinowski, Pawel Jerzy
PATENT ASSIGNEE(S):	Institute of Cancer Research, UK
SOURCE:	PCT Int. Appl., 28 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9306119	A1	19930401	WO 1992-GB1777	19920928

W: JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE

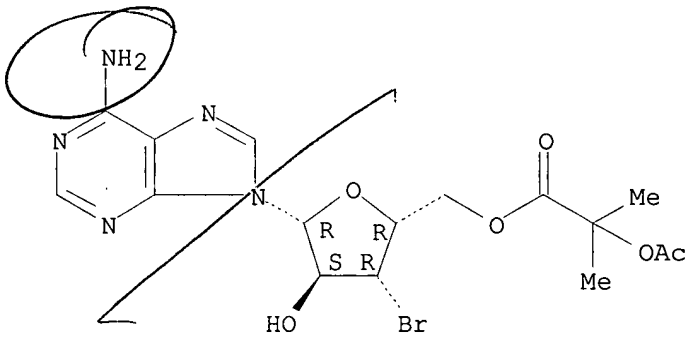
PRIORITY APPLN. INFO.: GB 1991-20533 19910927
GB 1992-7818 19920409

AB 2',3'-Didehydro-2',3'-deoxynucleosides (I) are prepd. by reaction of a ribonucleoside with 2-acyloxyisobutyryl halide to give 2'-, 3'-halo-5'-O-dioxolane deriv. which is converted to an acyloxyisobutyl ester 2'(3')-acyloxy-3'(2')-halo deriv., which is then selectively deacylated at the 3'(2')-position and converting to the 5'-O-(2-acyloxyisobutyryl)-2',3'-didehydro-2',3'-dideoxynucleoside, followed by deacylation to remove the acyloxyisobutyryl protectant at the 5'-position. I can be hydrogenated to give the title compds. (no data). To adenosine in MeNO2 was added MeCO2C(COBr)CMe2 and the product converted in 4 steps to give 2',3'-didehydro-2',3'-dideoxyadenosine.

IT **142544-52-3P 142544-53-4P 142544-55-6P**
142544-56-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and acylation with phenylchlorothionoformate)

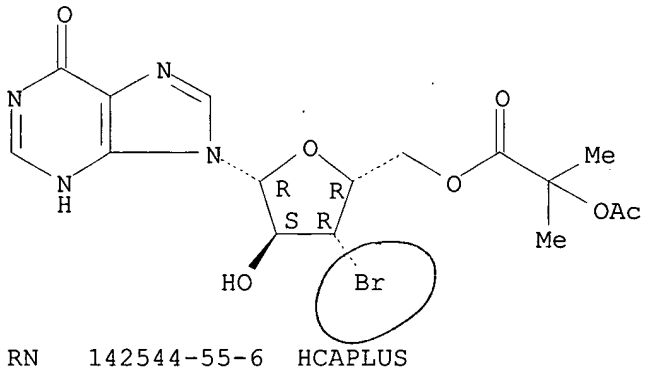
RN 142544-52-3 HCAPLUS
CN 9H-Purin-6-amine, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-3-bromo-3-deoxy-.beta.-D-xylofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



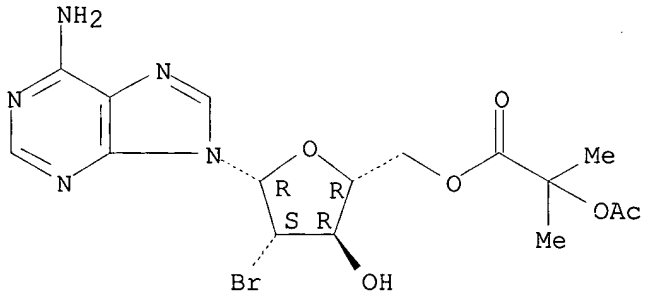
RN 142544-53-4 HCAPLUS
CN 6H-Purin-6-one, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-3-bromo-3-deoxy-.beta.-D-xylofuranosyl]-1,9-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



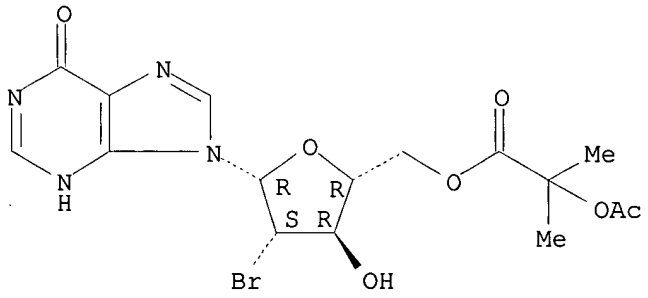
RN 142544-55-6 HCAPLUS
CN 9H-Purin-6-amine, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-bromo-2-deoxy-.beta.-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 142544-56-7 HCAPLUS
CN 6H-Purin-6-one, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-bromo-2-deoxy-.beta.-D-arabinofuranosyl]-1,9-dihydro- (9CI) (CA INDEX NAME)

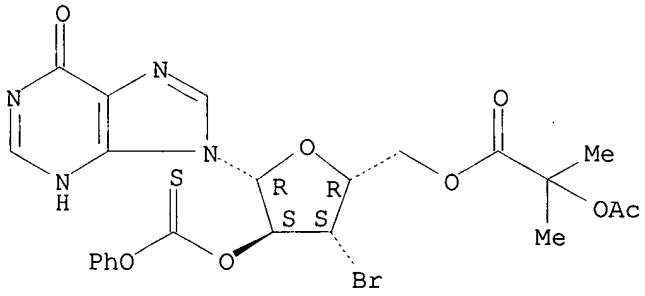
Absolute stereochemistry.



IT **142544-57-8P 142544-59-0P 142544-60-3P 142569-85-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and de(haloacylation), of)
RN 142544-57-8 HCAPLUS

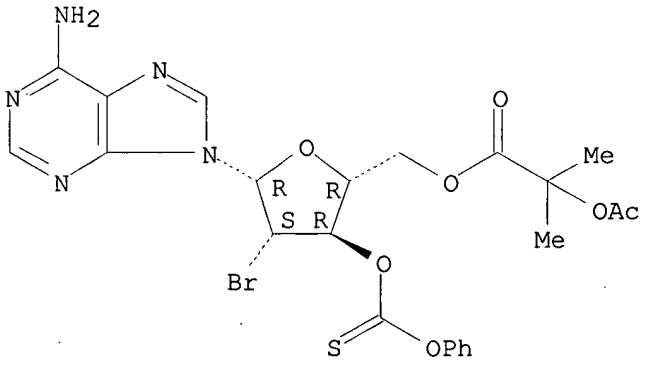
CN 6H-Purin-6-one, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-3-bromo-3-deoxy-2-O-(phenoxythioxomethyl)-.beta.-D-xylofuranosyl]-1,9-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



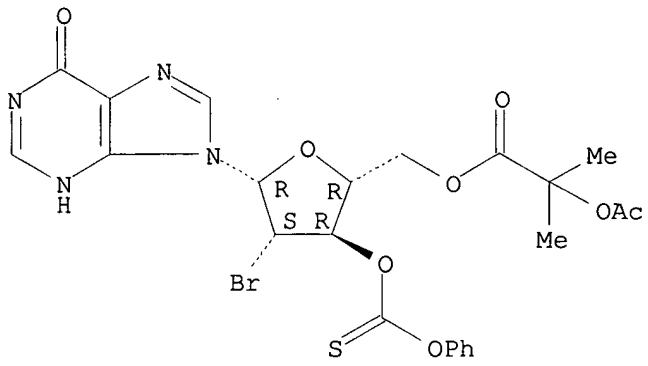
RN 142544-59-0 HCAPLUS
CN 9H-Purin-6-amine, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-bromo-2-deoxy-3-O-(phenoxythioxomethyl)-.beta.-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



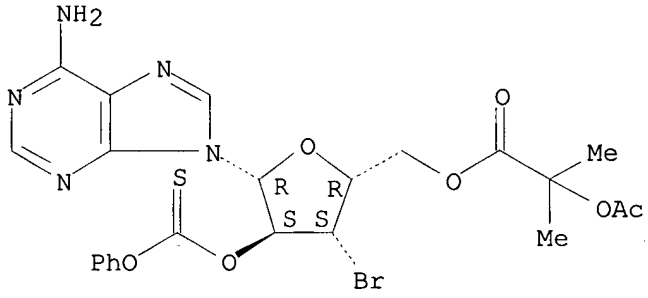
RN 142544-60-3 HCAPLUS
CN 6H-Purin-6-one, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-bromo-2-deoxy-3-O-(phenoxythioxomethyl)-.beta.-D-arabinofuranosyl]-1,9-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



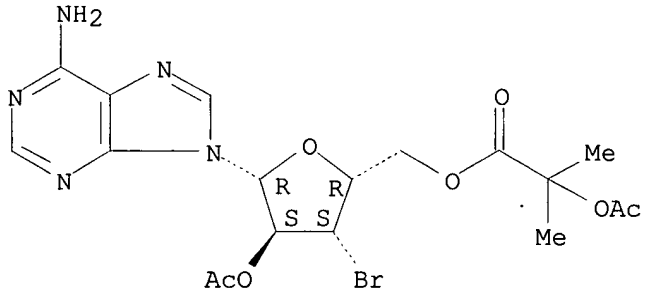
RN 142569-85-5 HCAPLUS
CN 9H-Purin-6-amine, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-3-bromo-3-deoxy-2-O-(phenoxythioxomethyl)-.beta.-D-xylofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



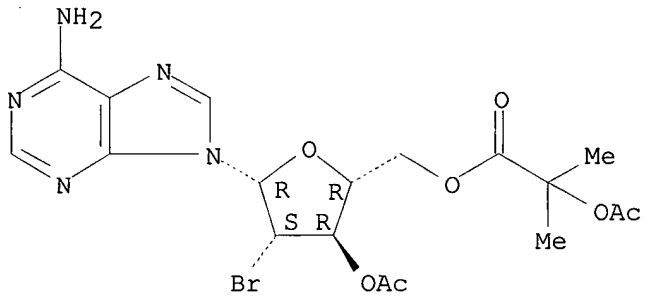
IT **122383-26-0P 122383-27-1P 122383-28-2P**
142544-49-8P 142544-50-1P 142544-61-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deacetylation of)
RN 122383-26-0 HCAPLUS
CN 9H-Purin-6-amine, 9-[2-O-acetyl-5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-3-bromo-3-deoxy-.beta.-D-xylofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

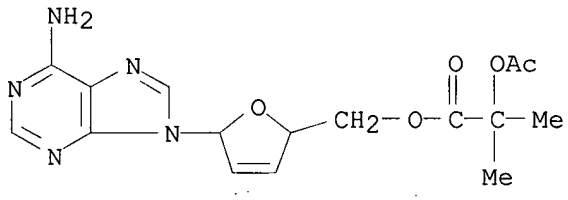


RN 122383-27-1 HCAPLUS
CN 9H-Purin-6-amine, 9-[3-O-acetyl-5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-bromo-2-deoxy-.beta.-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

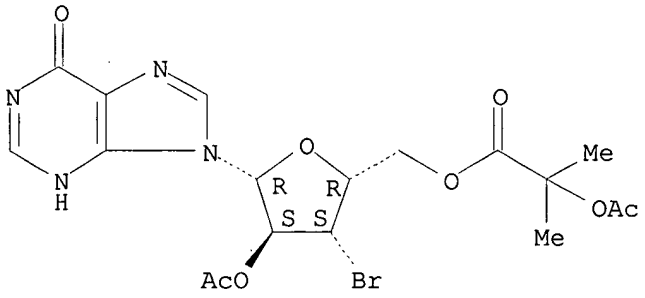


RN 122383-28-2 HCAPLUS
CN Adenosine, 2',3'-didehydro-2',3'-dideoxy-, 5'-[2-(acetyloxy)-2-methylpropanoate] (9CI) (CA INDEX NAME)



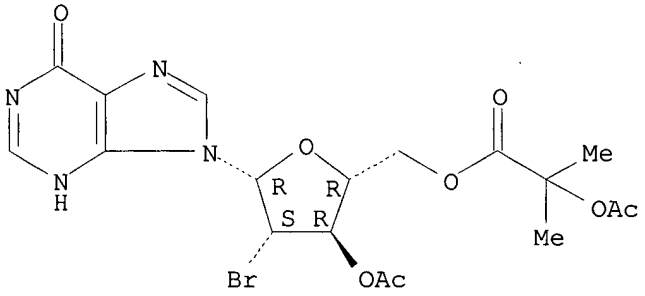
RN 142544-49-8 HCAPLUS
CN 6H-Purin-6-one, 9-[2-O-acetyl-5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-3-bromo-3-deoxy-.beta.-D-xylofuranosyl]-1,9-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

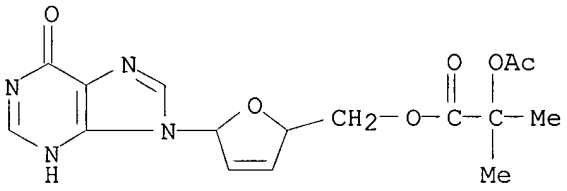


RN 142544-50-1 HCAPLUS
CN 6H-Purin-6-one, 9-[3-O-acetyl-5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-bromo-2-deoxy-.beta.-D-arabinofuranosyl]-1,9-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

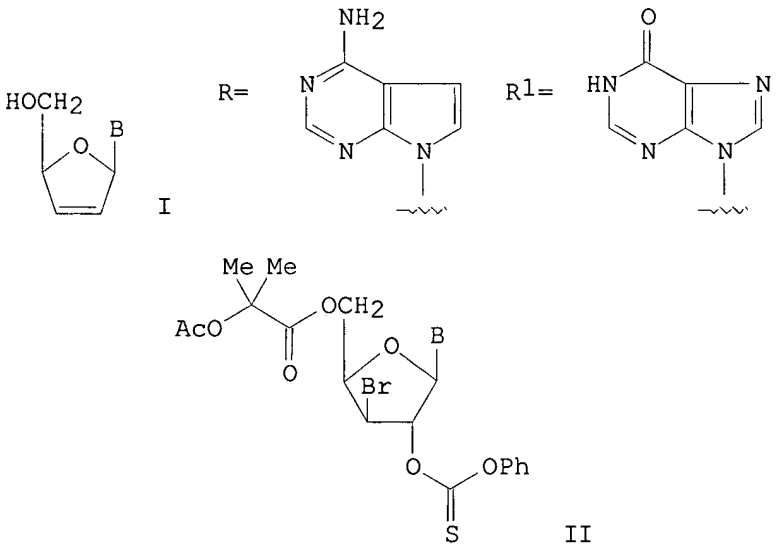


RN 142544-61-4 HCAPLUS
CN Inosine, 2',3'-didehydro-2',3'-dideoxy-, 5'-[2-(acetyloxy)-2-methylpropanoate] (9CI) (CA INDEX NAME)



L6 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:470212 HCAPLUS
DOCUMENT NUMBER: 117:70212
TITLE: A convenient method for the synthesis of 2',3'-didehydro-2',3'-dideoxy nucleosides
AUTHOR(S): Dorland, Erwin; Serafinowski, Pawel
CORPORATE SOURCE: Drug Dev. Sect., Inst. Cancer Res., Sutton/Surrey, SM2 5NG, UK
SOURCE: Synthesis (1992), (5), 477-81

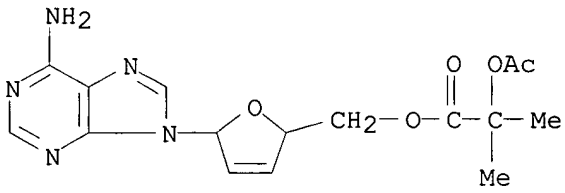
CODEN: SYNTBF; ISSN: 0039-7881
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 117:70212
GI



AB 2',3'-Didehydro-2',3'-dideoxy nucleosides I (B = R, R1, adenine) were prepd. via a free radical .beta.-elimination of bromo and phenoxy(thiocarbonyl) leaving groups from appropriate phenoxy(thiocarbonyl)bromo derivs. II, adenosine, inosine, and tubercidin with Bu3SnH and subsequent deprotection of the resulting 5'-O-(2-acetoxyisobutyryl)-2',3'-didehydro-2',3'-dideoxy-nucleosides.

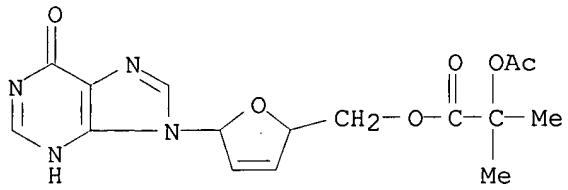
IT **122383-28-2P 142544-61-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deblocking of)

RN 122383-28-2 HCAPLUS
CN Adenosine, 2',3'-didehydro-2',3'-dideoxy-, 5'-[2-(acetyloxy)-2-methylpropanoate] (9CI) (CA INDEX NAME)



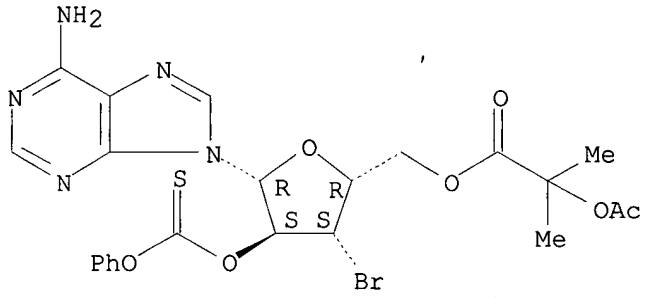
RN 142544-61-4 HCAPLUS
CN Inosine, 2',3'-didehydro-2',3'-dideoxy-, 5'-[2-(acetyloxy)-2-

methylpropanoate] (9CI) (CA INDEX NAME)



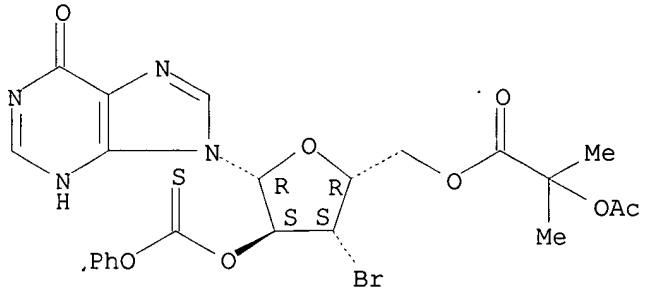
IT **142569-85-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and homolytic elimination reaction of)
RN 142569-85-5 HCAPLUS
CN 9H-Purin-6-amine, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-3-bromo-3-deoxy-2-O-(phenoxythioxomethyl)-.beta.-D-xylofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



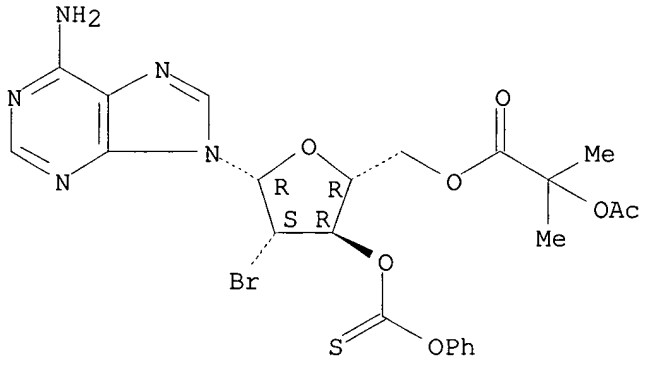
IT **142544-57-8P 142544-59-0P 142544-60-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and homolytic redn. of)
RN 142544-57-8 HCAPLUS
CN 6H-Purin-6-one, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-3-bromo-3-deoxy-2-O-(phenoxythioxomethyl)-.beta.-D-xylofuranosyl]-1,9-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



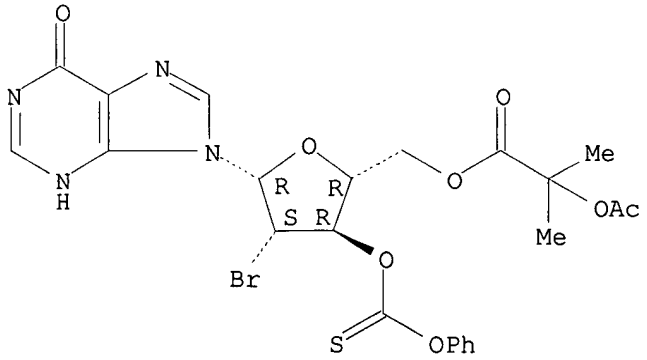
RN 142544-59-0 HCAPLUS
CN 9H-Purin-6-amine, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-bromo-2-deoxy-3-O-(phenoxythioxomethyl)-.beta.-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 142544-60-3 HCAPLUS
CN 6H-Purin-6-one, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-bromo-2-deoxy-3-O-(phenoxythioxomethyl)-.beta.-D-arabinofuranosyl]-1,9-dihydro- (9CI) (CA INDEX NAME)

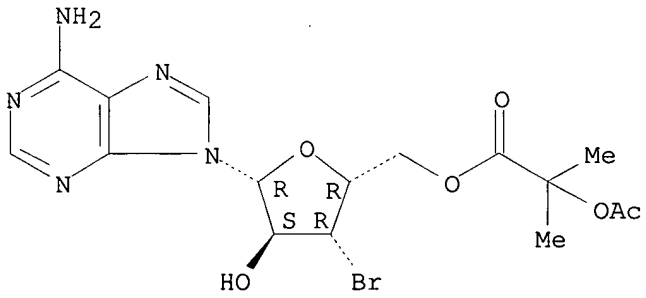
Absolute stereochemistry.



IT **142544-52-3P 142544-53-4P 142544-55-6P**
142544-56-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(prepn. and reaction of, with phenylchlorothionoformate)

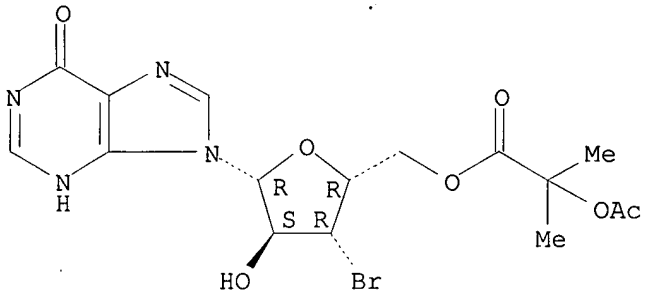
RN 142544-52-3 HCAPLUS
CN 9H-Purin-6-amine, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-3-bromo-3-deoxy-.beta.-D-xylofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



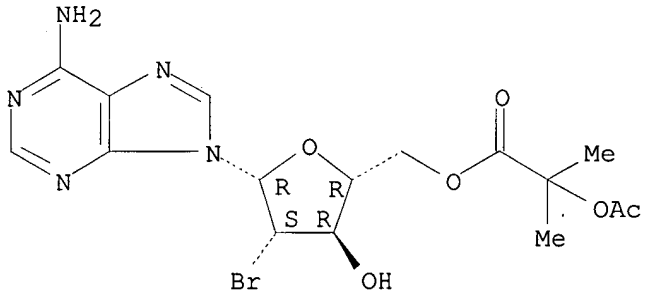
RN 142544-53-4 HCAPLUS
CN 6H-Purin-6-one, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-3-bromo-3-deoxy-.beta.-D-xylofuranosyl]-1,9-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



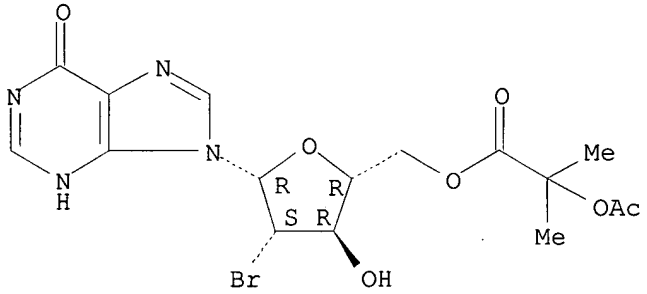
RN 142544-55-6 HCAPLUS
CN 9H-Purin-6-amine, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-bromo-2-deoxy-.beta.-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



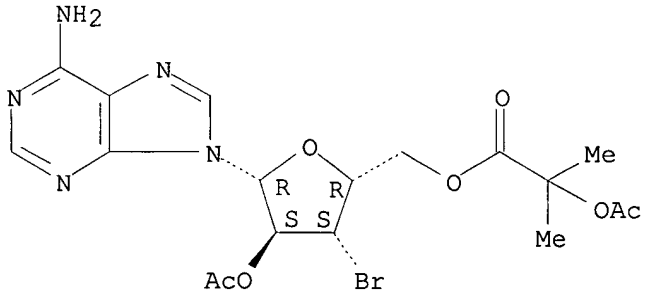
RN 142544-56-7 HCAPLUS
CN 6H-Purin-6-one, 9-[5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-bromo-2-deoxy-.beta.-D-arabinofuranosyl]-1,9-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



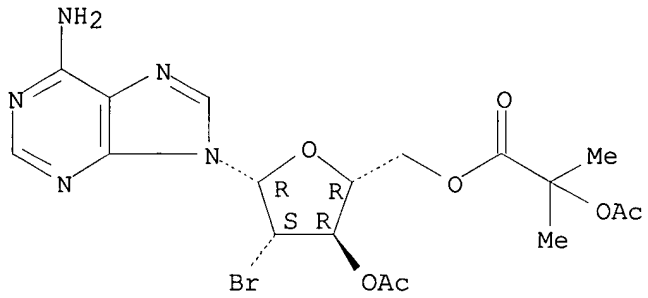
IT **122383-26-0P 122383-27-1P 142544-49-8P**
142544-50-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)
RN 122383-26-0 HCAPLUS
CN 9H-Purin-6-amine, 9-[2-O-acetyl-5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-3-bromo-3-deoxy-.beta.-D-xylofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



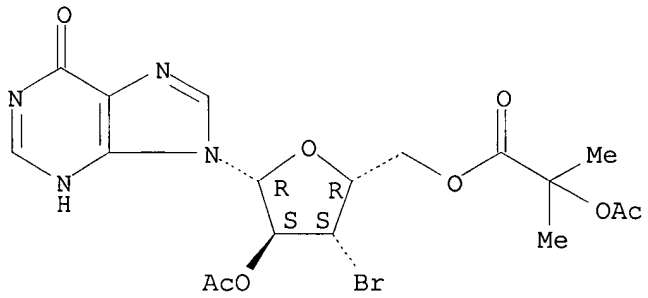
RN 122383-27-1 HCAPLUS
CN 9H-Purin-6-amine, 9-[3-O-acetyl-5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-bromo-2-deoxy-.beta.-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



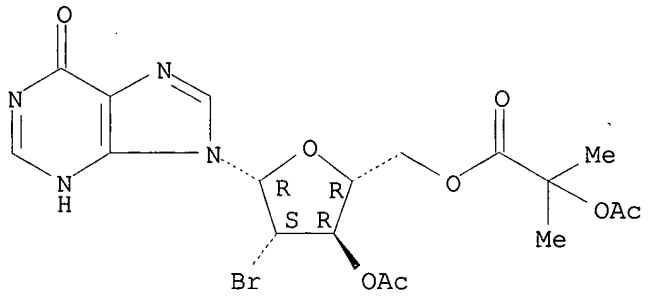
RN 142544-49-8 HCAPLUS
CN 6H-Purin-6-one, 9-[2-O-acetyl-5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-3-bromo-3-deoxy-.beta.-D-xylofuranosyl]-1,9-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 142544-50-1 HCAPLUS
CN 6H-Purin-6-one, 9-[3-O-acetyl-5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-bromo-2-deoxy-.beta.-D-arabinofuranosyl]-1,9-dihydro- (9CI) (CA INDEX NAME)

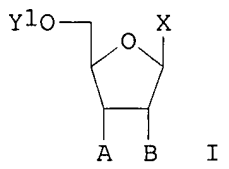
Absolute stereochemistry.



L6 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:515024 HCAPLUS
DOCUMENT NUMBER: 115:115024
TITLE: Preparation of (acyloxymethyl)dideoxy nucleosides as antivirals
INVENTOR(S): Klaveness, Jo; Undheim, Kjell; Rise, Frode; Hatlelid, Jostein; Holmes, Michael John
PATENT ASSIGNEE(S): Nycomed A/S, Norway
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9106554	A1	19910516	WO 1990-EP1853	19901106
W: AU, CA, FI, JP, NO, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 2073063	AA	19910507	CA 1990-2073063	19901106
AU 9066192	A1	19910531	AU 1990-66192	19901106
AU 636678	B2	19930506		
EP 500610	A1	19920902	EP 1990-916194	19901106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05501404	T2	19930318	JP 1990-514754	19901106
FI 9202014	A	19920505	FI 1992-2014	19920505
NO 9201776	A	19920703	NO 1992-1776	19920505

PRIORITY APPLN. INFO.: GB 1989-25037 19891106
GB 1989-25039 19891106
WO 1990-EP1853 19901106
OTHER SOURCE(S): MARPAT 115:115024
GI



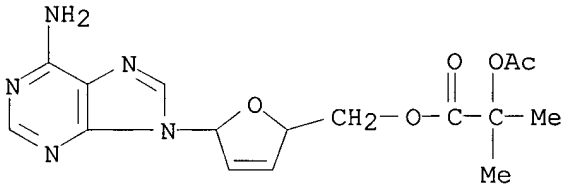
Searcher : Shears 308-4994

AB 2',3'-Dideoxynucleosides I [A = F and B = H or AB = bond; Y1 = H, R1(O)nCO(OCR2R3)m; m, n = 0, 1; R1 = (substituted) alkyl or aryl, N-(C1-7 alkyl)-1,4-dihydropyridin-3-yl or R1 = H when n = 0; R2, R3 = H, C1-6 alkyl; X = (substituted) purinyl or pyrimidinyl], useful as antivirals (no data), were prepd. Thus 1-(2',3'-dideoxy-.beta.-D-glyceropent-2-enofuranosyl)thymine was condensed with thexyldimethylsilyl chloride and the resulting compd. was treated with chloromethyl pivalate in DMF contg. K2CO3. Deprotection of the acyloxymethylated deriv. by Bu4NBF4 gave 3-(pivaloyloxymethyl)-1-(2',3'-dideoxy-.beta.-D-glyceropent-2-enofuranosyl)thymine. Formulation of I were prepd.

IT **122383-28-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with Et chloroformate)

RN 122383-28-2 HCAPLUS

CN Adenosine, 2',3'-didehydro-2',3'-dideoxy-, 5'-[2-(acetyloxy)-2-methylpropanoate] (9CI) (CA INDEX NAME)

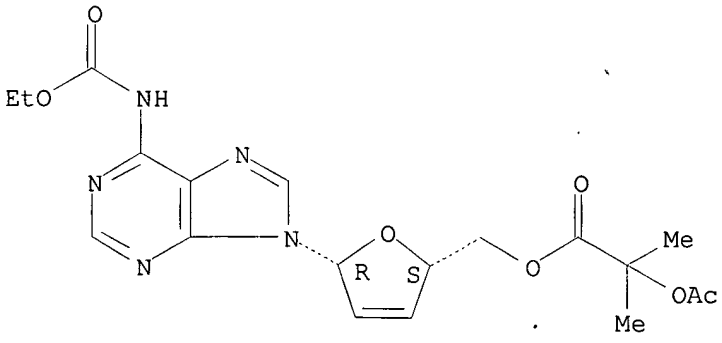


IT **135717-87-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deprotection of, in prepn. of antivirals)

RN 135717-87-2 HCAPLUS

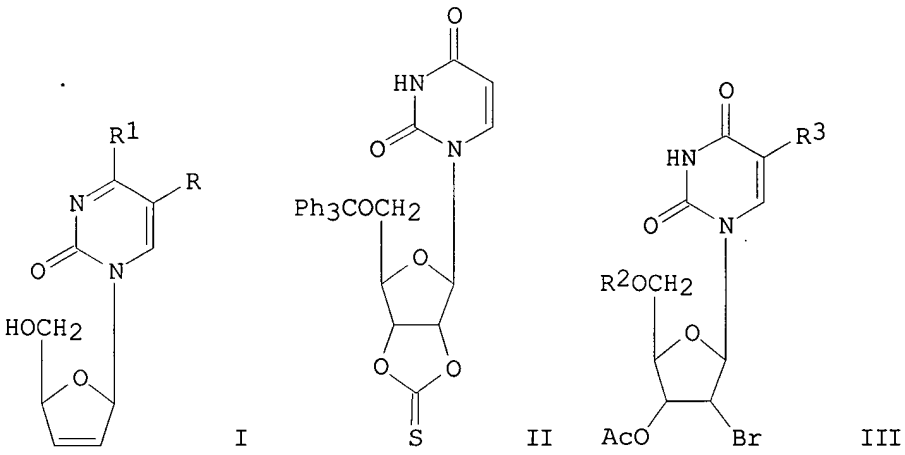
CN Propanoic acid, 2-(acetyloxy)-2-methyl-, [5-[6-[(ethoxycarbonyl)amino]-9H-purin-9-yl]-2,5-dihydro-2-furanyl]methyl ester, (2S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



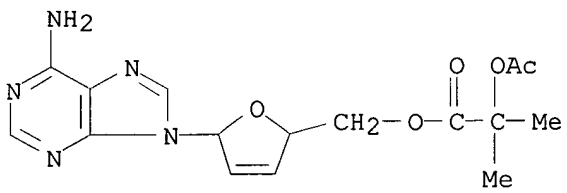
L6 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:554286 HCAPLUS

DOCUMENT NUMBER: 111:154286
TITLE: Preparation of 1-(2,3-dideoxy-.beta.-D-glycero-pent-2-enofuranosyl)thymine (d4T) and 2',3'-dideoxyadenosine (ddA): general methods for the synthesis of 2',3'-olefinic and 2',3'-dideoxy nucleoside analogs active against HIV
AUTHOR(S): Mansuri, Muzammil M.; Starrett, John E., Jr.; Wos, John A.; Tortolani, David R.; Brodfuehrer, Paul R.; Howell, Henry G.; Martin, John C.
CORPORATE SOURCE: Pharm. Res. Dev. Div., Bristol-Myers, Wallingford, CT, 06492-7660, USA
SOURCE: Journal of Organic Chemistry (1989), 54(20), 4780-5
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:154286
GI



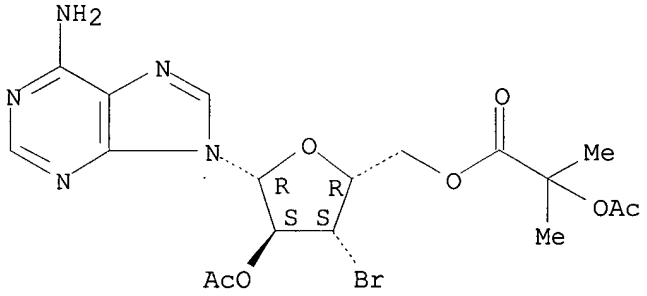
AB Methods for the prepn. of the 2',3'-unsatd. thymidine and cytidine analogs (I; R = Me, R1 = OH; R = H, R1 = NH2), 2',3'-dideoxycytidine and 2',3'-dideoxyadenosine, which are active in vitro against HIV, are reported. The methods used were the Corey-Winter reaction involving the fragmentation of a cyclic thionocarbonate II, olefin formation from 2',3'-O-alkoxymethylidene cyclic ortho esters, and the reductive elimination of the 2',3' halo acetates, e.g., III [R2 = COC(OAc)Me2, R3 = H, Me; R1 = Ac, R3 = Me). Of these 3 methods, the last was the most versatile, since the intermediates III or the trans-3'(2')-bromo-2'(3')-O-acetyl-3'(2')-deoxyarabinosylpurines are readily transformed to the corresponding olefins. As an example of the prepn. of a satd. 2',3'-dideoxy analog, 2',3'-dideoxyadenosine was obtained by catalytic redn. of the corresponding olefinic nucleoside.
IT **122383-28-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deacetylation of)

RN 122383-28-2 HCAPLUS
CN Adenosine, 2',3'-didehydro-2',3'-dideoxy-, 5'-[2-(acetyloxy)-2-methylpropanoate] (9CI) (CA INDEX NAME)



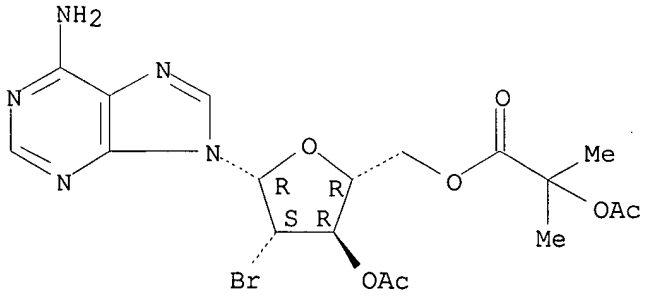
IT **122383-26-0P 122383-27-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and elimination reaction of)
RN 122383-26-0 HCAPLUS
CN 9H-Purin-6-amine, 9-[2-O-acetyl-5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-3-bromo-3-deoxy-.beta.-D-xylofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 122383-27-1 HCAPLUS
CN 9H-Purin-6-amine, 9-[3-O-acetyl-5-O-[2-(acetyloxy)-2-methyl-1-oxopropyl]-2-bromo-2-deoxy-.beta.-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

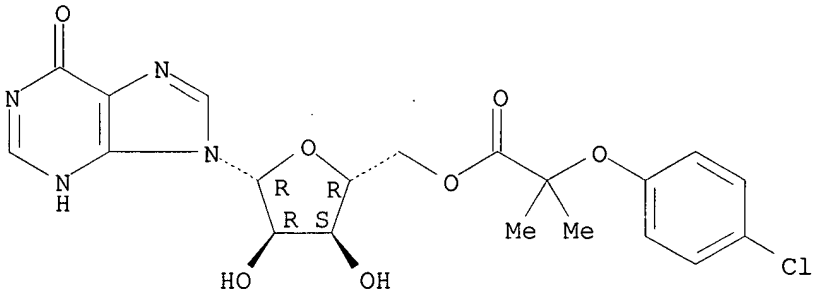


L6 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1974:520949 HCAPLUS
DOCUMENT NUMBER: 81:120949
TITLE: Inosine derivatives
INVENTOR(S): Hiraoka, Katsuyuki; Hirohashi, Mitsuru; Nagao, Koichiro; Miyoshi, Fumihiko
PATENT ASSIGNEE(S): Funai Pharmaceutical Industries, Ltd.
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 49070993	A2	19740709	JP 1972-112389	19721109
JP 55022480	B4	19800617		

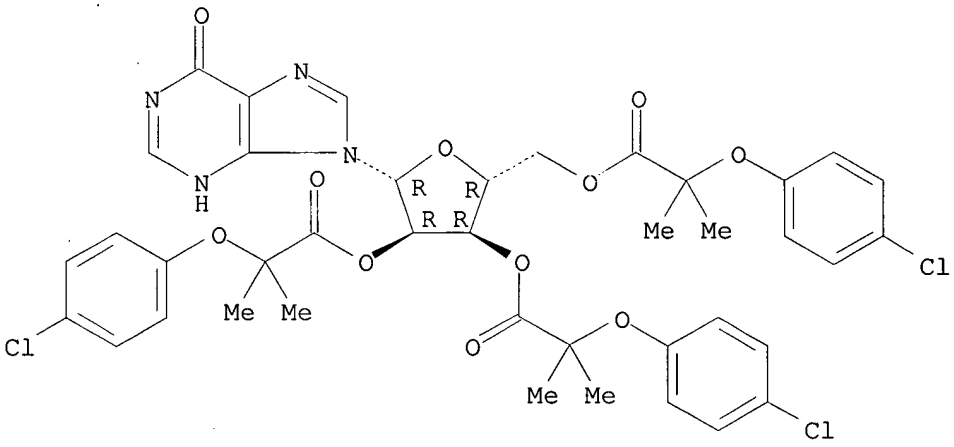
PRIORITY APPLN. INFO.: JP 1972-112389 19721109
GI For diagram(s), see printed CA Issue.
AB Inosine derivs. [I; R1-R3 = H or Q (R4 = H, halo; R5, R6 H, lower alkyl)] were prepd. by reacting I (R1-R3 = H or protecting groups, at least one is H) with .alpha.-(substituted phenoxy)alkylcarboxylic acids or their reactive derivs., QX (X = OH or reactive radicals), followed by removal of the protecting groups. I lowered serum cholesterol level. E.g., 20 g o-ClC6H4OCH2CO2-H was added to 27.5 g 2',3'-O-isopropylideneinosine in C5H5N, 22 g N,N'-dicyclohexylcarbodiimide added, and stirred 3 hr at 0.degree. and 3 hr at room temp. to give 24 g 2',3'-O-isopropylidene-5'-O-(o-chlorophenoxyacetyl)inosine (II). II, 2.4 g, with 3.5 ml 60% HCO2H 7 days at room temp. and SiO2-chromatog. gave 0.9 g 5'-O-[.alpha.-(o-chlorophenoxy)acetyl]inosine. Similarly, 5'-O-[.alpha.-(p-chlorophenoxy)isobutyroyl]-, 2',3',5'-O-tris(p-chlorophenoxy - acetyl)-, 2',3',5'-O-tris(.alpha.-phenoxybutyroyl)-, 2',3'-O-bis [.alpha.-(p-chlorophenoxy)isobutyroyl]-, and 2',3',5'-O-tris[.alpha.-(p-chlorophenoxy)isobutyroyl]inosines were prepd.
IT **53269-89-9P 53334-71-7P 54027-47-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 53269-89-9 HCAPLUS
CN Inosine, 5'-[2-(4-chlorophenoxy)-2-methylpropanoate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



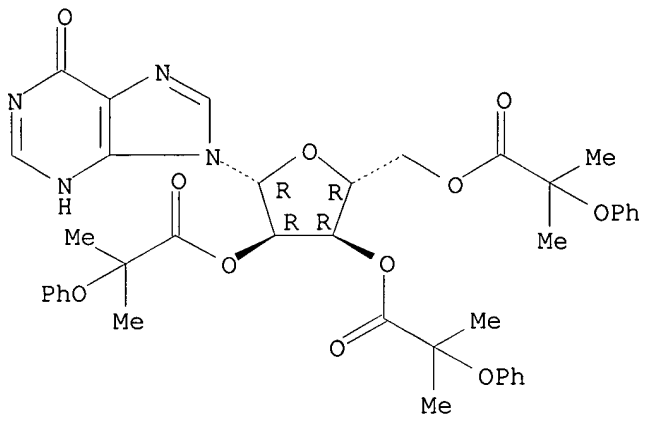
RN 53334-71-7 HCAPLUS
CN Inosine, 2',3',5'-tris[2-(4-chlorophenoxy)-2-methylpropanoate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 54027-47-3 HCAPLUS
CN Inosine, 2',3',5'-tris(2-methyl-2-phenoxypropanoate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

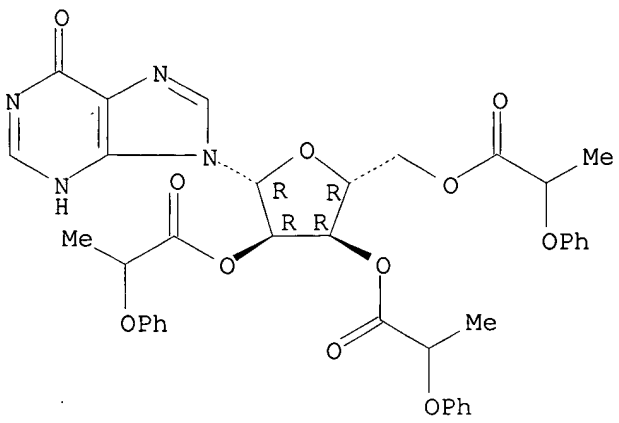


L6 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1974:491851 HCAPLUS
DOCUMENT NUMBER: 81:91851
TITLE: Hypolipidemic agents. II. Syntheses and hypolipidemic activities of phenoxyacetylinosine derivatives
AUTHOR(S): Miyoshi, Fumihiko; Hiraoka, Katsuyuki; Hirohashi, Mitsuru; Nagao, Koichiro; Sakakibara, Eiichi
CORPORATE SOURCE: Funai Gen. Res. Cent., Hirakata, Japan
SOURCE: Yakugaku Zasshi (1974), 94(3), 397-403
CODEN: YKKZAJ; ISSN: 0031-6903
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Mono-, bis-, and tris-.omicron.-(substituted phenoxyacetyl)-inosines were prepd. and assayed for hypolipidemic activities in rats. PMR spectra led to the assignment of C-proton on the ribose ring. The structure of 3',5'-.omicron.-bis[.alpha.-(p-chlorophenoxy)iso-butyryl]inosine was confirmed by the shift of C-3' and C-5' proton to lower field.

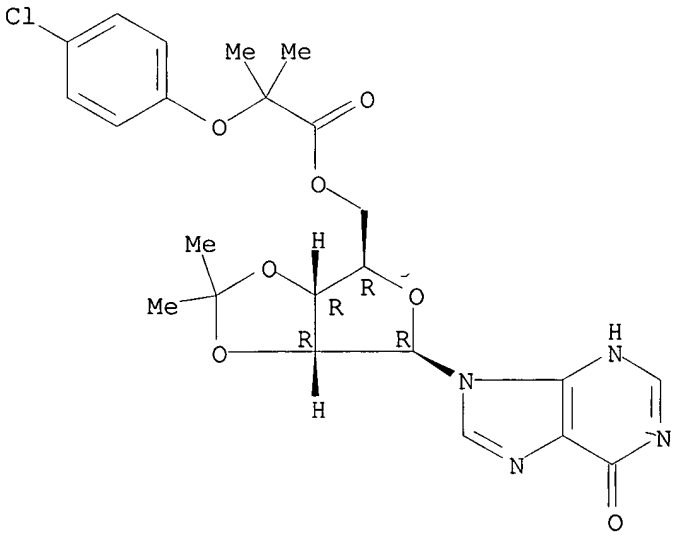
IT **53269-93-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and NMR studies of)
RN 53269-93-5 HCAPLUS
CN Inosine, 2',3',5'-tris(2-phenoxypropanoate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



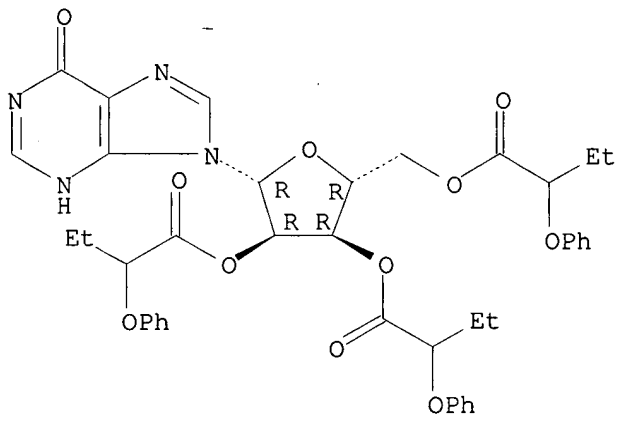
IT **53269-88-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deblocking of)
RN 53269-88-8 HCAPLUS
CN Inosine, 2',3'-O-(1-methylethylidene)-, 5'-[2-(4-chlorophenoxy)-2-methylpropanoate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



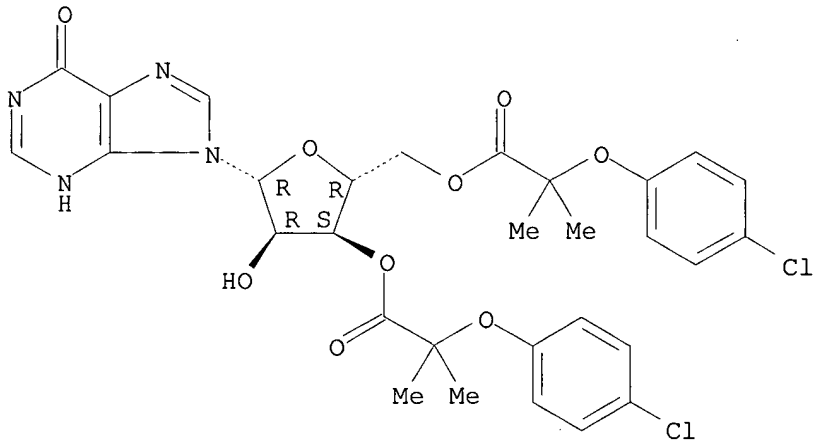
IT **53276-30-5P 53397-88-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 53276-30-5 HCAPLUS
CN Inosine, 2',3',5'-tris(2-phenoxybutanoate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



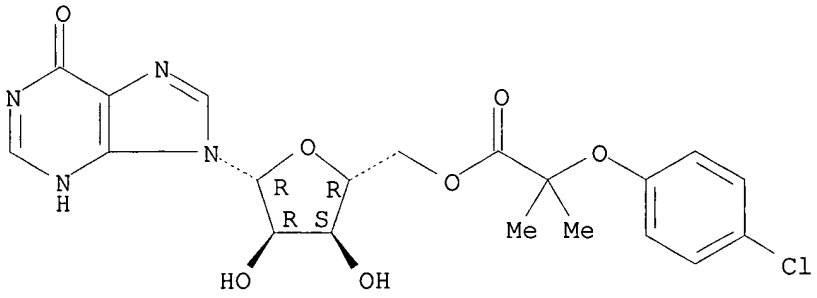
RN 53397-88-9 HCAPLUS
CN Inosine, 3',5'-bis[2-(4-chlorophenoxy)-2-methylpropanoate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



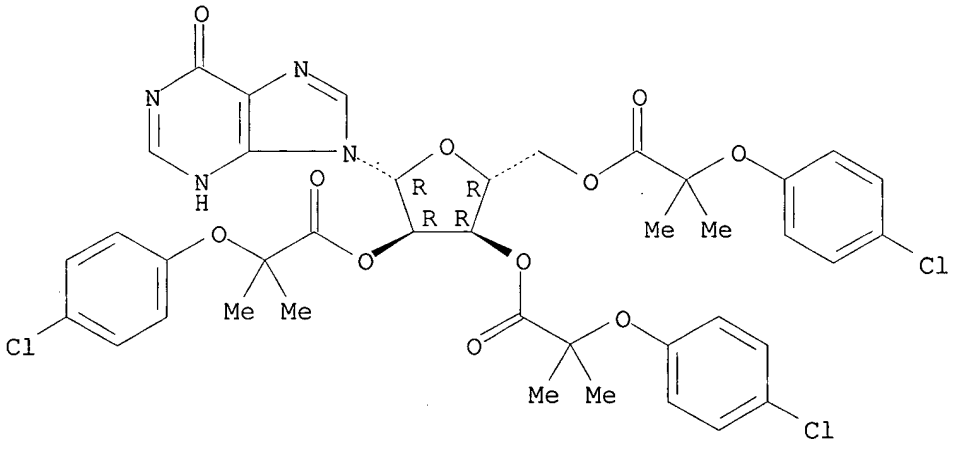
IT **53269-89-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., NMR, and hypolipidemic studies of)
RN 53269-89-9 HCAPLUS
CN Inosine, 5'-[2-(4-chlorophenoxy)-2-methylpropanoate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **53334-71-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., NMR, and partial deblocking of)
RN 53334-71-7 HCAPLUS
CN Inosine, 2',3',5'-tris[2-(4-chlorophenoxy)-2-methylpropanoate] (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



=> d his l7-; d ibib abs

(FILE 'HCAPLUS' ENTERED AT 11:20:19 ON 03 APR 2003)

FILE 'CAOLD' ENTERED AT 11:21:47 ON 03 APR 2003
L7 0 S L5

FILE 'USPATFULL' ENTERED AT 11:21:55 ON 03 APR 2003
L8 1 S L5

L8 ANSWER 1 OF 1 USPATFULL
ACCESSION NUMBER: 95:73623 USPATFULL
TITLE: 2'3'-dideoxy-2',3'-didehydro-7,8-disubstituted

guanosines and their immunostimulative effect

INVENTOR(S): Goodman, Michael G., Rancho Santa Fe, CA, United States
Chen, Robert, Belle Mead, NJ, United States
Reitz, Allen, Lansdale, PA, United States
PATENT ASSIGNEE(S): The Scripps Research Institute, La Jolla, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5441942		19950815	
APPLICATION INFO.:	US 1994-250483		19940527	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Robinson, Douglas W.
ASSISTANT EXAMINER: Crane, L. Eric
LEGAL REPRESENTATIVE: Welsh & Katz, Ltd.
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1,9
LINE COUNT: 861

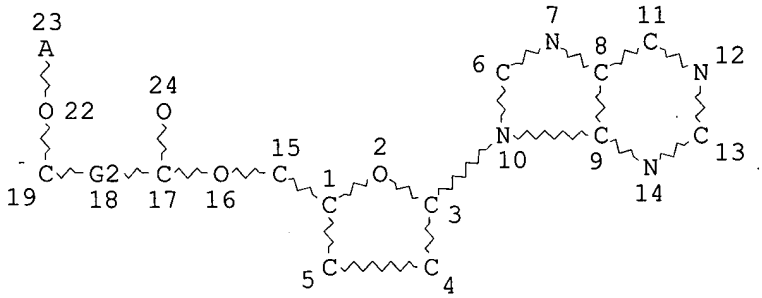
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Immunostimulating 7,8-disubstituted guanine derivatives that also contain a .beta.-9,1'-linked-2',3'-dideoxy-2',3'-didehydroribosyl substituent are disclosed whose structures are represented by Formula I ##STR1## wherein X is O or S; R.sup.1 is a hydrocarbyl or substituted hydrocarbyl moiety having a length of about one to about seven carbon atoms; R.sup.2 is hydrogen or C.sub.1 -C.sub.8 acyl; and the pharmaceutically acceptable base addition salts thereof. Also disclosed are compositions containing an immunostimulating guanine derivative and processes for using the same.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

(FILE 'MARPAT' ENTERED AT 11:22:45 ON 03 APR 2003)

L15 STR



REP G2=(0-5) CH2
NODE ATTRIBUTES:
NSPEC IS RC AT 23
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L17 44 SEA FILE=MARPAT SSS FUL L15 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 1012 ITERATIONS 44 ANSWERS
SEARCH TIME: 00.00.14

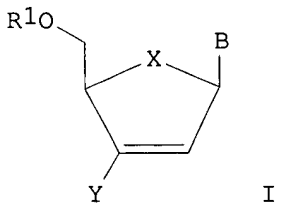
L17 ANSWER 1 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 138:56191 MARPAT
TITLE: Preparation, antiviral activity, and cytotoxicity of .beta.-2'- and 3'-halo-nucleosides
INVENTOR(S): Chu, Chung K.; Otto, Michael J.; Shi, Junxing; Schinazi, Raymond F.; Choi, Yongseok; Gumina, Giuseppe; Chong, Youhoon
PATENT ASSIGNEE(S): Pharmasset Ltd., Barbados; University of Georgia Research Foundation, Inc.; Emory University
SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000200	A2	20030103	WO 2002-US20245	20020624

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-300356P 20010622
US 2001-305386P 20010713

GI



I

AB The present invention includes compds. and compns. of .beta.-halo-nucleosides I wherein: R1 is hydrogen, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO- alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, amino acid residue, mono, di, or triphosphate, or a phosphate deriv.; X is O, S, SO2 or CH2; Y is fluoro, chloro, bromo or iodo; and B is a purine or pyrimidine base that may optionally be substituted, as well as methods to treat HIV, HBV or abnormal cellular proliferation comprising administering said compds. or compns. Thus, (-)-1-[(1S,4R)-2,3-dideoxy-2,3-didehydro-2-fluoro-4-thio-.beta.-D-ribofuranosyl]-cytosine was prepd. and tested in vitro as antiviral agent. Preferred examples of antiviral agents can be used in combination or alternation with other known antiviral agents for HIV therapy. Use of the any one of the pharmaceutical compns. for the treatment and/or prophylaxis of an HIV infection or an abnormal cellular proliferation in a host.

IC ICM A61K

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 63

ST human antiviral nucleoside prodrug AIDS cytotoxicity prepn cellular proliferation

IT Cell proliferation
(inhibition; prepn., antiviral activity, and cytotoxicity of .beta.-2'- and 3'-halo-nucleosides)

IT Anti-AIDS agents
Antiviral agents
Cytotoxic agents
Cytotoxicity
Hepatitis B virus
Human
Human immunodeficiency virus 1
Therapy
(prepn., antiviral activity, and cytotoxicity of .beta.-2'- and 3'-halo-nucleosides)

IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn., antiviral activity, and cytotoxicity of .beta.-2'- and 3'-halo-nucleosides)

IT Nucleosides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn., antiviral activity, and cytotoxicity of .beta.-2'- and 3'-halo-nucleosides)

IT Drug delivery systems
(prodrugs; prepn., antiviral activity, and cytotoxicity of .beta.-2'- and 3'-halo-nucleosides)

IT Infection
(viral; prepn., antiviral activity, and cytotoxicity of .beta.-2'- and 3'-halo-nucleosides)

IT 9026-93-1, Adenosine deaminase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn., antiviral activity, and cytotoxicity of .beta.-2'- and 3'-halo-nucleosides)

IT 125362-05-2P 165399-47-3P 166249-15-6P 396653-01-3P
398133-37-4P 476210-28-3P 476210-30-7P 476210-37-4P
479036-01-6P 479036-12-9P 479036-22-1P 479036-23-2P
479036-25-4P 479036-26-5P 479036-38-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn., antiviral activity, and cytotoxicity of .beta.-2'- and 3'-halo-nucleosides)

IT 3056-17-5, D4T 7481-89-2, DDC 30516-87-1, AZT 39809-25-1, Penciclovir 59277-89-3, Acyclovir 69655-05-6, DDI 104227-87-4, Famciclovir 118353-05-2, Carbovir 127779-20-8, Saquinavir 129618-40-2, Nevirapine 136470-78-5, Abacavir 143491-54-7, FTC 145440-12-6 145514-01-8 145514-04-1 149950-60-7, MKC-442 150378-17-9, Indinavir 154598-52-4, DMP-266 163252-36-6, L-FMAU 177932-89-7, DMP-450 181623-96-1 181785-94-4 182967-46-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn., antiviral activity, and cytotoxicity of .beta.-2'- and 3'-halo-nucleosides)

IT 609-06-3, L-Xylose 15186-48-8 26661-13-2 34837-55-3, Benzeneselenenyl bromide 137719-21-2 169736-17-8 180675-22-3 212954-52-4 367491-78-9 479036-27-6 479036-29-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn., antiviral activity, and cytotoxicity of .beta.-2'- and 3'-halo-nucleosides)

IT 68660-45-7P 145887-01-0P 145887-10-1P 145887-11-2P
171721-11-2P 184700-37-6P 395075-12-4P 395075-13-5P
395075-14-6P 395075-15-7P 395075-16-8P 395075-17-9P
395075-18-0P 395075-19-1P 395075-20-4P 395075-21-5P
398133-29-4P 398133-32-9P 398133-34-1P 398133-35-2P
398133-36-3P 476209-84-4P 476209-86-6P 476209-92-4P
476209-94-6P 476210-00-1P 476210-02-3P 476210-04-5P
476210-06-7P 476210-09-0P 476210-11-4P 476210-22-7P
476210-24-9P 476210-26-1P 476210-32-9P 476210-33-0P
476210-34-1P 476210-35-2P 476210-39-6P 476210-45-4P
476210-47-6P 479035-76-2P 479035-77-3P 479035-78-4P
479035-79-5P 479035-80-8P 479035-81-9P 479035-82-0P
479035-83-1P 479035-84-2P 479035-85-3P 479035-86-4P
479035-89-7P 479035-90-0P 479035-91-1P 479035-92-2P
479035-93-3P 479035-94-4P 479035-95-5P 479035-96-6P
479035-98-8P 479036-13-0P 479036-14-1P 479036-15-2P
479036-16-3P 479036-17-4P 479036-18-5P 479036-19-6P
479036-20-9P 479036-21-0P 479036-30-1P 479036-31-2P
479036-32-3P 479036-40-3P 479036-41-4P 479036-42-5P
479036-43-6P 479036-44-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., antiviral activity, and cytotoxicity of .beta.-2'- and 3'-halo-nucleosides)

IT 396653-02-4P 398133-33-0P 479035-87-5P 479035-88-6P
479036-03-8P 479036-05-0P 479036-28-7P 479036-39-0P
479036-45-8P 479036-46-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., antiviral activity, and cytotoxicity of .beta.-2'- and 3'-halo-nucleosides)

L17 ANSWER 2 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:217180 MARPAT
TITLE: Method for the synthesis of 2',3'-dideoxy-2',3'-didehydronucleosides
INVENTOR(S): Jin, Fuqiang; Confalone, Pasquale N.

PATENT ASSIGNEE(S): Pharmasset Ltd., USA
SOURCE: PCT Int. Appl., 180 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070533	A2	20020912	WO 2002-US6460	20020301
WO 2002070533	A3	20021219		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002198224	A1	20021226	US 2002-87112	20020301
PRIORITY APPLN. INFO.:			US 2001-272434P	20010301
			US 2001-272441P	20010301

OTHER SOURCE(S): CASREACT 137:217180

AB The present invention is an efficient synthetic route to 2',3'-dideoxy-2',3'-didehydro-nucleosides from available precursors with the option of introducing functionality as needed, such as, the 2',3'-dideoxy- and 2'- or 3'-deoxyribo-nucleoside analogs as well as addnl. derivs. obtained by subsequent functional group manipulations. Briefly, the present invention discloses a method for the prepn. of .beta.-D- and .beta.-L-2',3'-dideoxy-2',3'-didehydro-nucleosides starting from appropriately substituted ribonucleosides in two, optionally three steps: step (1) a halo-acylation, such as halo-acetylation, and in particular, bromo-acetylation; step (2) a reductive elimination; and optionally, step (3) a deprotection. The halo-acylation of step (1) can form the 2'-acyl-3'-halo-nucleoside, the 3'-acyl-2'-halo-nucleoside, or a mixt. thereof.

IC ICM C07H019-00
CC 33-9 (Carbohydrates)
ST deoxydidehydronucleoside synthesis solvent effect redn halogenation acylation elimination
IT Elimination reaction
(reductive; synthesis and solvent effect of 2',3'-dideoxy-2',3'-didehydronucleosides via halo-acetylation and reductive elimination reactions)
IT Acetylation
Halogenation
Solvent effect
(synthesis and solvent effect of 2',3'-dideoxy-2',3'-didehydronucleosides via halo-acetylation and reductive elimination reactions)
IT Nucleosides, preparation
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and solvent effect of 2',3'-dideoxy-2',3'-didehydronucleosides via halo-acetylation and reductive elimination reactions)

IT 221156-23-6P 457065-01-9P 457065-03-1P 457065-09-7P 457065-13-3P 457065-15-5P 457065-20-2P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and solvent effect of 2',3'-dideoxy-2',3'-didehydronucleosides via halo-acetylation and reductive elimination reactions)

IT 15379-29-0P 40635-67-4P 74595-08-7P 107232-40-6P 107232-53-1P 134379-77-4P 181785-84-2P 221156-21-4P 457065-17-7P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis and solvent effect of 2',3'-dideoxy-2',3'-didehydronucleosides via halo-acetylation and reductive elimination reactions)

IT 316-46-1, 5-Fluorouridine 1681-53-4 2341-22-2, 5-Fluorocytidine 457065-22-4 457065-24-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and solvent effect of 2',3'-dideoxy-2',3'-didehydronucleosides via halo-acetylation and reductive elimination reactions)

IT 91-65-6, N,N-Diethylcyclohexylamine 98-94-2, N,N-Dimethylcyclohexylamine 102-82-9, Tributylamine 109-02-4, N-Methylmorpholine 110-18-9 110-86-1, Pyridine, reactions 121-44-8, Triethylamine, reactions 280-57-9, 1,4-Diazabicyclo[2.2.2]octane 3001-72-7, 1,5-Diazabicyclo[4.3.0]non-5-ene 5683-33-0 6674-22-2, 1,8-Diazabicyclo[5.4.0]undec-7-ene 7087-68-5, N,N-Diisopropylethylamine 7378-99-6, N,N-Dimethyloctylamine
RL: RGT (Reagent); RACT (Reactant or reagent)
(synthesis and solvent effect of 2',3'-dideoxy-2',3'-didehydronucleosides via halo-acetylation and reductive elimination reactions)

L17 ANSWER 3 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:185764 MARPAT
TITLE: Preparation of amino acid-containing .beta.-L-2'-deoxy-nucleosides as antiviral agents for the treatment of hepatitis B
INVENTOR(S): Gosselin, Gilles; Imbach, Jean-louis; Bryant, Martin L.
PATENT ASSIGNEE(S): Novirio Pharmaceuticals Limited, Cyprus; Centre National Da La Recherche Scientifique
SOURCE: U.S., 31 pp., Cont.-in-part of U.S. 6,395,716.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6444652	B1	20020903	US 1999-459150	19991210
US 6395716	B1	20020528	US 1999-371747	19990810
PRIORITY APPLN. INFO.:			US 1998-96110P	19980810

US 1999-131352P 19990428
US 1999-371747 19990810

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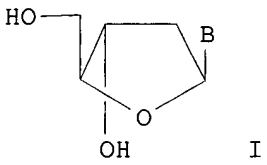


I

AB This invention is directed to a method for treating a host infected with hepatitis B comprising administering an effective amt. of an anti-HBV biol. active 2'-deoxy-.beta.-L-erythro-pentofuranonucleoside or a pharmaceutically acceptable salt or prodrug thereof, wherein the 2'-deoxy-.beta.-L-erythro-pentofuranonucleoside has the formula I: wherein R is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, amino acid residue, mono, di, or triphosphate, or a phosphate deriv.; and B is a purine or pyrimidine base which may be optionally substituted. The 2'-deoxy-.beta.-L-erythro-pentofuranonucleoside or a pharmaceutically acceptable salt or prodrug thereof may be administered either alone or in combination with another 2'-deoxy-.beta.-L-erythro-pentofuranonucleoside or in combination with another anti-hepatitis B agent. Thus, 2'-deoxy-.beta.-L-cytidine (.beta.-L-dC) was prepd. as antiviral agents for the treatment of hepatitis B. The inhibition of hepatitis B replication in 2.2.15 cells by .beta.-L-dA and .beta.-L-dC, alone and in combination was measured (EC50 = 0.0005-0.5 .mu.M).

IC ICM A61K031-70
NCL 514045000
CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 34, 63

ST human cytotoxicity nucleoside nucleotide amino acid prepn antiviral; nucleoside nucleotide amino acid prepn antiviral hepatitis prodrug resistance

IT Hepatitis
(B; prepn. of .beta.-L-2'-deoxy-nucleosides as antiviral agents for the treatment of hepatitis B)

IT Antiviral agents
Human
Multidrug resistance
(prepn. of .beta.-L-2'-deoxy-nucleosides as antiviral agents for the treatment of hepatitis B)

IT Amino acids, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .beta.-L-2'-deoxy-nucleosides as antiviral agents for the treatment of hepatitis B)

IT Drug delivery systems
(prodrugs; prepn. of .beta.-L-2'-deoxy-nucleosides as antiviral agents for the treatment of hepatitis B)

IT Infection
(viral; prepn. of .beta.-L-2'-deoxy-nucleosides as antiviral agents for the treatment of hepatitis B)
IT 40093-94-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of .beta.-L-2'-deoxy-nucleosides as antiviral agents for the treatment of hepatitis B)
IT 377736-64-6 377736-66-8 377736-67-9 377736-68-0 449753-71-3
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(prepn. of .beta.-L-2'-deoxy-nucleosides as antiviral agents for the treatment of hepatitis B)
IT 14365-45-8P 179112-93-7P 449753-66-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .beta.-L-2'-deoxy-nucleosides as antiviral agents for the treatment of hepatitis B)
IT 31501-19-6 36791-04-5, Ribavirin 39809-25-1, Penciclovir 82410-32-0, Ganciclovir 104227-87-4, Famciclovir 106941-25-7, 9-[2-(Phosphonomethoxy)ethyl]adenine 127759-89-1, Lobucavir 134678-17-4, 3TC 142217-69-4, Entecavir 143491-54-7, FTC 145514-04-1, ..beta..-D-2,6-Diaminopurine dioxolane 163252-36-6 189639-16-5 198632-86-9 258854-64-7 449753-67-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of .beta.-L-2'-deoxy-nucleosides as antiviral agents for the treatment of hepatitis B)
IT 609-06-3, L-Xylose 922-67-8, Methyl propiolate 1005-56-7, Phenoxythiocarbonyl chloride 1873-77-4, Tris(trimethylsilyl)silane 5328-37-0, L-Arabinose 154463-66-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of .beta.-L-2'-deoxy-nucleosides as antiviral agents for the treatment of hepatitis B)
IT 3080-30-6P 31501-46-9P 31615-96-0P 31615-98-2P 31615-99-3P 35939-60-7P 40093-85-4P 40093-93-4P 154463-68-0P 216571-43-6P 216571-44-7P 233681-07-7P 233681-08-8P 233681-09-9P 258529-64-5P 258529-65-6P 258529-66-7P 258529-67-8P 258529-68-9P 449753-62-2P 449753-64-4P 449753-65-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of .beta.-L-2'-deoxy-nucleosides as antiviral agents for the treatment of hepatitis B)
REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

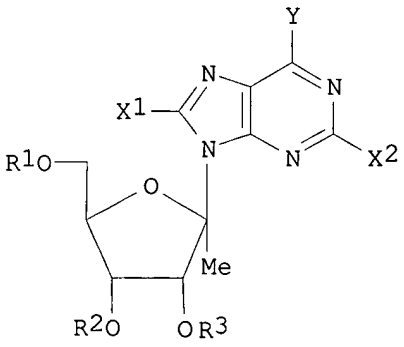
L17 ANSWER 4 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:6296 MARPAT
TITLE: Preparation of antiviral nucleosides and methods for treating hepatitis C virus
INVENTOR(S): Sommadossi, Jean-Pierre; Lacolla, Paulo
PATENT ASSIGNEE(S): Novirio Pharmaceuticals Limited, Cayman I.; Universita degli Studi di Cagliari

SOURCE: PCT Int. Appl., 296 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001090121	A2	20011129	WO 2001-US16671	20010523
WO 2001090121	A3	20020502		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001074906	A5	20011203	AU 2001-74906	20010523
US 2003050229	A1	20030313	US 2001-864078	20010523
EP 1292603	A2	20030319	EP 2001-941564	20010523
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2002005627	A	20030106	NO 2002-5627	20021122

PRIORITY APPLN. INFO.: US 2000-206585P 20000523
WO 2001-US16671 20010523

GI



I

AB A method and compn. for treating a host infected with hepatitis C comprising administering an effective hepatitis C treatment amt. of a described 1'-, 2'- or 3'-modified nucleosides I, wherein : R1-R3 and R are independently H, phosphate (including mono, di- or triphosphate and a stabilized phosphate prodrug); acyl; alkyl; sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the Ph group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other

pharmaceutically acceptable leaving group which when administered in vivo is capable of providing a compd. wherein R1-R3 are independently H or phosphate; Y is hydrogen, bromo, chloro, fluoro, iodo, OR4, NR4R5 or SR4; X1 and X2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR4, NR4R5 or SR4; and R4 and R5 are independently hydrogen, acyl, alkyl.or a pharmaceutically acceptable salt or prodrug thereof, is provided. Thus, I (R1-R3 = X1 = X2 = H, Y = NH2) was prepd. and tested in Cynomolgus monkeys as antiviral agent. Oral bioavailability in monkeys, bone human bone marrow toxicity (IC50 > 10 .mu.M), and mitochondrial toxicity, were reported .

IC ICM C07H
CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 15, 63
ST nucleoside antiviral prepn bone marrow mitochondrial toxicity
IT Hepatitis
(C; prepn. of antiviral nucleosides and methods for treating hepatitis C virus)
IT Antiviral agents
Bone marrow
Drug bioavailability
Mitochondria
Toxicity
(prepn. of antiviral nucleosides and methods for treating hepatitis C virus)
IT Nucleosides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of antiviral nucleosides and methods for treating hepatitis C virus)
IT 36791-04-5, Ribavirin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of antiviral nucleosides and methods for treating hepatitis C virus)
IT 15397-12-3P 16848-12-7P 20724-73-6P 31448-54-1P 34441-68-4P 38946-83-7P 38946-84-8P 54401-19-3P 69123-98-4P 119410-84-3P 125911-76-4P 374750-27-3P 374750-28-4P 374750-29-5P 374750-30-8P 374750-31-9P 374750-32-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of antiviral nucleosides and methods for treating hepatitis C virus)

L17 ANSWER 5 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:590 MARPAT
TITLE: Methods and compositions using modified nucleosides for treating flaviviruses and pestiviruses
INVENTOR(S): Sommadossi, Jean-Pierre; Lacolla, Paolo
PATENT ASSIGNEE(S): Novirio Pharmaceuticals Limited, Cayman I.; Universita Degli Studi Di Cagliari
SOURCE: PCT Int. Appl., 302 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001092282	A2	20011206	WO 2001-US16687	20010523
WO 2001092282	A3	20020502		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1294735	A2	20030326	EP 2001-952131	20010523
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003060400	A1	20030327	US 2001-863816	20010523
NO 2002005600	A	20030117	NO 2002-5600	20021121
PRIORITY APPLN. INFO.:			US 2000-207674P	20000526
			US 2001-283276P	20010411
			WO 2001-US16687	20010523

AB A method and compn. are provided for treating a host infected with flavivirus or pestivirus, comprising administering an effective amt. of a 1', 2' or 3'-modified nucleoside or a pharmaceutically acceptable salt or prodrug thereof.

IC ICM C07H019-00
CC 1-5 (Pharmacology)
Section cross-reference(s): 63
ST flavivirus pestivirus antiviral nucleoside deriv
IT Drug delivery systems
(capsules; nucleoside derivs. for treating flaviviruses and pestiviruses)
IT Toxicity
(drug; nucleoside derivs. for treating flaviviruses and pestiviruses)
IT Hematopoietic precursor cell
(erythroid burst-forming; nucleoside derivs. for treating flaviviruses and pestiviruses)
IT Hematopoietic precursor cell
(granulocyte-macrophage colony-forming; nucleoside derivs. for treating flaviviruses and pestiviruses)
IT Mitochondria
(mitochondrial toxicity; nucleoside derivs. for treating flaviviruses and pestiviruses)
IT Toxicity
(myelotoxicity; nucleoside derivs. for treating flaviviruses and pestiviruses)
IT Antiviral agents
Bovine diarrhea virus
Cytotoxicity

Drug bioavailability
Flavivirus
Pestivirus
(nucleoside derivs. for treating flaviviruses and pestiviruses)

IT Drug delivery systems
(tablets; nucleoside derivs. for treating flaviviruses and pestiviruses)

IT Bone marrow
(toxicity; nucleoside derivs. for treating flaviviruses and pestiviruses)

IT Drug delivery systems
(unit doses; nucleoside derivs. for treating flaviviruses and pestiviruses)

IT 15397-12-3 16848-12-7 20724-73-6 31448-54-1 69123-98-4, FIAU 119410-84-3 374750-30-8 374750-32-0
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleoside derivs. for treating flaviviruses and pestiviruses)

IT 125911-76-4 374750-27-3 374750-28-4 374750-29-5
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)
(nucleoside derivs. for treating flaviviruses and pestiviruses)

IT 34441-68-4 38946-83-7 38946-84-8 54401-19-3 374750-31-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleoside derivs. for treating flaviviruses and pestiviruses)

L17 ANSWER 6 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 135:335139 MARPAT
TITLE: Pharmaceutical composition of modified PNA molecules
INVENTOR(S): Christensen, Jeppe Viggo; Kristensen, Edward
PATENT ASSIGNEE(S): Pantheco A/S, Den.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001076636	A2	20011018	WO 2001-DK238	20010406
WO 2001076636	A3	20020228		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1296718	A1	20030402	EP 2001-921241	20010406

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,

PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: DK 2000-587 20000406
DK 2000-5 20000406
WO 2001-DK238 20010406

AB The present invention concerns a peptide nucleic acid pharmaceutical compn. for use in combating infections.

IC ICM A61K047-48

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 10, 33, 34

ST antibiotic peptide nucleic acid infection

IT Anti-infective agents
Antibacterial agents
Buffers
Drug bioavailability
Enterococcus faecium
Escherichia coli
Klebsiella pneumoniae
Micrococcus luteus
Preservatives
Pseudomonas aeruginosa
Salmonella typhimurium
Staphylococcus aureus
Surfactants
Thickening agents
(anti-infective pharmaceutical compn. of modified PNA mols.)

IT Antisense oligonucleotides
Peptide nucleic acids
Peptides, biological studies
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-infective pharmaceutical compn. of modified PNA mols.)

IT Peptides, biological studies
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antisense; anti-infective pharmaceutical compn. of modified PNA mols.)

IT Drug delivery systems
(carriers; anti-infective pharmaceutical compn. of modified PNA mols.)

IT Drug delivery systems
(injections; anti-infective pharmaceutical compn. of modified PNA mols.)

IT Drug delivery systems
(parenterals; anti-infective pharmaceutical compn. of modified PNA mols.)

IT 56-12-2, 4-Aminobutanoic acid, reactions 56-40-6, Glycine, reactions 56-91-7, 4-Aminomethylbenzoic acid 60-32-2, 6-Aminohexanoic acid 107-95-9, .beta.-Alanine 327-57-1, Norleucine 949-99-5 1132-68-9 1776-53-0, 4-Aminocyclohexylcarboxylic acid 2935-35-5 2952-01-4, cis-4-Aminocyclohexaneacetic acid 3685-23-2 6600-40-4, Norvaline 14328-51-9, Cyclohexylglycine 27527-05-5 34702-59-5 55750-61-3 55750-63-5 58626-38-3 64987-85-5 79886-55-8 92625-28-0, Aminododecanoic acid 102735-53-5 125559-00-4 134978-97-5 367927-39-7
RL: PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(PNA linker; anti-infective pharmaceutical compn. of modified PNA

mols.)
IT 335473-24-0P 335688-54-5P
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-infective pharmaceutical compn. of modified PNA mols.)
IT 335688-69-2P 368507-45-3P 368950-86-1P 368950-88-3P
368950-89-4P 368950-90-7P 368950-91-8P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-infective pharmaceutical compn. of modified PNA mols.)
IT 335240-18-1 335473-27-3 368951-41-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(anti-infective pharmaceutical compn. of modified PNA mols.)
IT 368951-43-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-infective pharmaceutical compn. of modified PNA mols.)
IT 137638-48-3 180205-53-2 335240-08-9 335240-09-0 335240-10-3
335240-11-4 335240-13-6 335240-14-7 335240-15-8 335240-16-9
335240-17-0 368454-06-2 368454-07-3 368454-08-4 368454-09-5
368454-10-8 368454-11-9 368454-12-0 368454-13-1
RL: PRP (Properties)
(unclaimed sequence; pharmaceutical compn. of modified PNA mols.)

L17 ANSWER 7 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:361343 MARPAT
TITLE: Compositions and methods for double-targeting virus infections and targeting cancer cells
INVENTOR(S): Kucera, Louis S.; Fleming, Ronald A.; Ishaq, Khalid S.; Kucera, Gregory L.; Morris-Natschke, Susan L.
PATENT ASSIGNEE(S): Wake Forest University, USA; The University of North Carolina at Chapel Hill
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034614	A2	20010517	WO 2000-US41352	20001020
WO 2001034614	A3	20011227		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1228080	A2	20020807	EP 2000-989666	20001020
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: US 1999-162290P 19991028

WO 2000-US41352 20001020

AB The invention includes compns. and methods useful for treatment of a virus infection in a mammal by double-targeting the virus (i.e. targeting the virus at more than one stage of the virus life cycle) and thereby inhibiting virus replication. The compns. of the invention include compds. which comprise a phosphocholine moiety covalently conjugated with one or more antiviral agents (e.g. nucleoside analog, protease inhibitor, etc.) to a lipid backbone. The invention also includes pharmaceutical compns. and kits for use in treatment of a virus infection in mammals. The methods of the invention comprise administering a compd. of the invention, a pharmaceutically acceptable salt thereof, or a pharmaceutical compn. of the invention, in an amt. effective to treat the infection, to a mammal infected with a virus. Addnl., the invention includes compns. and methods useful for combating a cancer in a mammal and for facilitating delivery of a therapeutic agent to a mammalian cell. The compns. of the invention include compds. which comprise an alkyl lipid or phospholipid moiety covalently conjugated with an anticancer agent (e.g. a nucleoside analog). The invention also includes pharmaceutical compns. and kits for combating a cancer and for facilitating delivery of a therapeutic agent to a mammalian cell. The methods of the invention comprise administering a compd. of the invention, a pharmaceutically acceptable salt thereof, or a pharmaceutical compn. of the invention, in an amt. effective to combat a cancer or to facilitate delivery of a therapeutic agent to a mammalian cell.

IC ICM C07F009-02
CC 1-5 (Pharmacology)
Section cross-reference(s): 33, 63
ST phosphocholine antiviral agent conjugate cancer treatment; phospholipid anticancer agent conjugate virus infection

IT Antitumor agents
(carcinoma; compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT Nervous system
(central, disease, treatment; compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT Nervous system
(central, drug delivery to; compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT Anti-AIDS agents
Antitumor agents
Antiviral agents
Cytomegalovirus
Cytotoxicity
Drug delivery systems
Hepatitis A virus
Hepatitis B virus
Hepatitis C virus
Hepatitis E virus
Hepatitis delta virus
Hepatitis virus
Human herpesvirus
Human herpesvirus 1
Human herpesvirus 2

Human herpesvirus 3
Human herpesvirus 4
Human herpesvirus 6
Human herpesvirus 7
Human herpesvirus 8
Human immunodeficiency virus
Human immunodeficiency virus 1
Human immunodeficiency virus 2
(compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT Phospholipids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates with anticancer and antiviral agents; compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT Nucleoside analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates with phospholipids; compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT Cardiovascular system
Lymphatic system
Reproductive tract
(disease, treatment; compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT Astrocyte
Lymphocyte
Neuroglia
(drug delivery to; compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT Antitumor agents
(leukemia; compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT Antitumor agents
(lymphoma; compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT Nerve, neoplasm
(neuroblastoma, inhibitors; compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT Antitumor agents
(neuroblastoma; compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT Antitumor agents
(sarcoma; compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT Antitumor agents
(solid tumor; compns. and methods for double-targeting virus

infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT Brain, disease
Kidney, disease
Liver, disease
(treatment; compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT 9068-38-6
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HIV-1, inhibition; compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT 340130-53-2, BM 21-1290
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT 340130-56-5P, INK 18
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT 340130-55-4, INK 17
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT 340130-57-6, INK 20 340130-58-7, INK 21 340130-59-8, INK 22
340130-60-1, INK 23 340130-61-2, INK 24 340130-62-3, INK 25
340130-63-4, INK 26 340130-64-5, INK 19
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT 29706-85-2, AZT monophosphate 92586-35-1, AZT triphosphate
106060-89-3, AZT diphosphate
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT 30516-87-1, AZT
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); RCT (Reactant); BIOL (Biological study); FORM (Formation, nonpreparative); RACT (Reactant or reagent)
(compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT 1663-67-8, Malonyl chloride

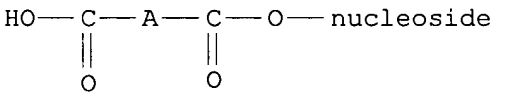
RL: RCT (Reactant); RACT (Reactant or reagent)
(compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

IT 313343-77-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(compns. and methods for double-targeting virus infections and targeting cancer cells in relation to cytotoxicity and metab.)

L17 ANSWER 8 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:56917 MARPAT
TITLE: Preparation of nucleosides as antiviral agents
INVENTOR(S): Vlieghe, Patrick; Kraus, Jean-Louis; Clerc, Thierry; Salles, Jean-Pierre
PATENT ASSIGNEE(S): Laboratoires Laphal S.A., Fr.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077020	A1	20001221	WO 2000-FR1630	20000613
W: AL, AU, BR, CA, CN, CZ, HU, IL, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SI, US, VN				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
FR 2794752	A1	20001215	FR 1999-7411	19990611
PRIORITY APPLN. INFO.:			FR 1999-7411	19990611

GI



I

AB Nucleosides I wherein A represents a divalent group selected among -(CH2)n-, -(CH2)n-NH-, -(CH2)n-O- or a divalent arom. group; n is an integer ranging between 1 and 12; and the nucleoside group is selected among the group consisting of zidovudine, didanosine (dideoxyinosine), and stavudine, were prepd. as antiviral agents. Thus, 3'-azido-3'-deoxy-5'-O-(malonyl)thymidine was prepd. and tested for its antiviral activity (EC50 = 0.01 .mu.M).

IC ICM C07H019-06
ICS C07H019-16; A61K031-70; A61P031-18

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 63

ST zidovudine didanosine stavudine nucleoside prepn antiviral

IT Antiviral agents
(prepn. of nucleosides as antiviral agents)

IT Nucleosides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU

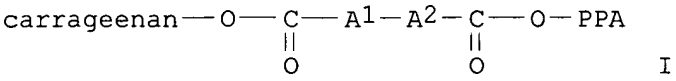
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of nucleosides as antiviral agents)
IT 3056-17-5, d4t 30516-87-1, Azt 69655-05-6, 2',3'-Dideoxy-inosine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(prepn. of nucleosides as antiviral agents)
IT 106060-83-7P 128305-54-4P 142894-17-5P 152336-78-2P
256390-94-0P 256390-95-1P 256390-97-3P 313340-94-2P
313341-08-1P 313341-17-2P 313341-29-6P 313341-34-3P
313343-77-0P 313343-78-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of nucleosides as antiviral agents)
IT 56-12-2, 4-Aminobutanoic acid, reactions 75-65-0,
2-Methyl-2-propanol, reactions 100-21-0, Terephthalic acid,
reactions 108-30-5, Succinic anhydride, reactions 108-55-4,
Glutaric anhydride 110-63-4, 1,4-Butanediol, reactions 111-16-0,
Pimelic acid 118-41-2, 3,4,5-Trimethoxybenzoic acid, reactions
124-04-9, Adipic acid, reactions 505-48-6, Suberic acid
821-38-5, 1,12-Dodecane dicarboxylic acid 4379-33-3,
tert-Butylmalonic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of nucleosides as antiviral agents)
IT 5105-78-2P 5105-79-3P 50479-22-6P 313343-76-9P 313343-80-5P
313343-81-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of nucleosides as antiviral agents)
IT 313343-79-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of nucleosides as antiviral agents)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 9 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:56916 MARPAT
TITLE: Preparation of nucleoside-carrageenan conjugates as antiviral and antitumor agents
INVENTOR(S): Vlieghe, Patrick; Kraus, Jean-Louis; Clerc, Thierry; Salles, Jean-Pierre
PATENT ASSIGNEE(S): Laboratoires Laphal S.A., Fr.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077019	A1	20001221	WO 2000-FR1629	20000613

W: AL, AU, BR, CA, CN, CZ, HU, IL, JP, KR, LT, LV, MK, MX, NO,

NZ, PL, RO, RU, SI, US, VN
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
FR 2794753 A1 20001215 FR 1999-7413 19990611
FR 2794753 B1 20010914
PRIORITY APPLN. INFO.: FR 1999-7413 19990611
GI



I

AB The invention concerns the field of org. chem. and more particularly that of therapeutic chem. More precisely, the invention concerns the prepn. of compds. derived from carrageenan of general formula I wherein the carrageenan group represents .kappa.-, .iota.-, and .lambda.-carrageenan, A1 represents a single bond or a divalent group -NH- or a group -O-; A2 represents a divalent aliph. group -(CH2)n-, -(CH2)n- NH-, -(CH2)n-O-, an alkyl chain substituted by a hydroxyl or a divalent arom. group, optionally substituted by a hydroxyl group; n is an integer ranging between 1 and 12, and PPA represents the dehydroxylated radical of a mol. of an active principle having antiviral properties and having a functional hydroxyl group capable of being substituted. The compds. of formula I are used as active principles in pharmaceutical compns., in particular with antiviral activity. Thus, conjugate of 3'-azido-3'-deoxy-5'-O-(succinyl)thymidinoate and .kappa.-carrageenan was prepd. and tested in vitro for its antiviral activity (EC30 = 4 .mu.g/mL) and antitumor activity (cell poliferation CC50 > 200 .mu.g/mL).

IC ICM C07H019-06
ICS C07H019-16; A61K031-70; A61P031-18
CC 33-9 (Carbohydrates)
ST nucleoside carrageenan polysaccharide conjugate prepn antiviral antitumor

IT Antitumor agents
Antiviral agents
(prepn. of nucleoside-carrageenan conjugates as antiviral and antitumor agents)

IT Nucleosides, preparation
Polysaccharides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of nucleoside-carrageenan conjugates as antiviral and antitumor agents)

IT 3056-17-5, d4T 30516-87-1, AZT 69655-05-6, DdI
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(prepn. of nucleoside-carrageenan conjugates as antiviral and antitumor agents)

IT 313467-50-4P 313467-51-5P 313467-52-6P 313467-53-7P
313467-54-8P 313467-55-9P 313467-56-0P 313467-58-2P
313467-59-3P 313467-60-6P 313467-61-7P 313467-62-8P
313467-63-9P 313467-65-1P 313467-67-3P 313467-70-8P
313467-72-0P 313467-75-3P 313474-66-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of nucleoside-carrageenan conjugates as antiviral and antitumor agents)

IT 108-30-5, Succinic anhydride, reactions 108-55-4, Glutaric anhydride 111-16-0, Pimelic acid 124-04-9, Adipic acid, reactions 505-48-6, Suberic acid 4521-61-3, 3,4,5-Trimethoxybenzoic acid chloride 9064-57-7, .lambda.-Carrageenan 11114-20-8, .kappa.-Carrageenan 313341-29-6 313341-34-3
313341-35-4 313341-36-5 313341-37-6 313341-39-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of nucleoside-carrageenan conjugates as antiviral and antitumor agents)

IT 106060-83-7P 128305-54-4P 142894-17-5P 152336-78-2P
256390-94-0P 313340-78-2P 313340-81-7P 313340-85-1P
313340-89-5P 313340-94-2P 313340-98-6P 313341-05-8P
313341-08-1P 313341-12-7P 313341-17-2P 313341-21-8P
313341-25-2P 313341-32-1P 313467-64-0P 313467-77-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of nucleoside-carrageenan conjugates as antiviral and antitumor agents)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

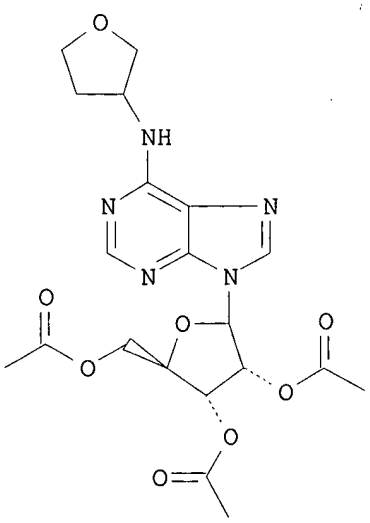
L17 ANSWER 10 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:21461 MARPAT
TITLE: Orally active A1 adenosine receptor agonists
INVENTOR(S): Blackburn, Brent K.; Melville, Chris; Zablocki, Jeff A.; Palle, Venkata P.; Elzein, Elfatih O.; Wang, Lisa
PATENT ASSIGNEE(S): CV Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000071558	A1	20001130	WO 2000-US14036	20000519

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,

BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 2002091099 A1 20020711 US 1999-317523 19990524
EP 1181302 A1 20020227 EP 2000-932688 20000519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
BR 2000010882 A 20020611 BR 2000-10882 20000519
NO 2001005662 A 20020123 NO 2001-5662 20011120
PRIORITY APPLN. INFO.: US 1999-317523 19990524
WO 2000-US14036 20000519

GI



I

AB A substituted N6-oxa, thia, thioxa and azacycloalkyl substituted adenosine deriv. and a method for using the compn. as an A1 adenosine receptor agonist are presented. The therapeutically effective amt. of an A1 adenosine receptor agonist ranges from 0.01-100 mg/kg. For example, an adenosine prodrug I was prepd. and administered to rats in an oral gavage at a dose of 0.5 mg/kg. A rapid onset of the drug was obsd. based on the decrease in heart rate which was between 100-150 beats/min. Theophylline, a non-specific antagonist of all of the adenosine receptor subtypes, reversed the I effects on heart rate, indicating involvement of adenosine receptors.

IC ICM C07H019-16
ICS A61K031-70; A61P009-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 33
ST adenosine deriv prepn oral purinoceptor agonist; prodrug adenosine heterocyclic deriv purinoceptor agonist; cardiovascular agent tachycardia oral purinoceptor agonist
IT Purinoceptor agonists
(A1; oral A1 adenosine receptor agonists for treatment of tachycardia)
IT Heart, disease
(atrial fibrillation; oral A1 adenosine receptor agonists for

treatment of tachycardia)

IT Heart, disease
(atrial flutter; oral A1 adenosine receptor agonists for treatment of tachycardia)

IT Cardiovascular agents
Heart rate
(oral A1 adenosine receptor agonists for treatment of tachycardia)

IT Adenosine receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(oral A1 adenosine receptor agonists for treatment of tachycardia)

IT Drug delivery systems
(oral; oral A1 adenosine receptor agonists for treatment of tachycardia)

IT Drug delivery systems
(prodrugs; oral A1 adenosine receptor agonists for treatment of tachycardia)

IT Drug delivery systems
(solns., oral; oral A1 adenosine receptor agonists for treatment of tachycardia)

IT Heart, disease
(supraventricular tachycardia; oral A1 adenosine receptor agonists for treatment of tachycardia)

IT Drug delivery systems
(tablets; oral A1 adenosine receptor agonists for treatment of tachycardia)

IT Heart, disease
(tachycardia, AV nodal re-entrant tachycardia; oral A1 adenosine receptor agonists for treatment of tachycardia)

IT 309724-86-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(oral A1 adenosine receptor agonists for treatment of tachycardia)

IT 204512-90-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(oral A1 adenosine receptor agonists for treatment of tachycardia)

IT 309724-88-7P 309724-90-1P 309724-92-3P 309724-94-5P
309724-96-7P 309724-98-9P 309725-00-6P 309725-02-8P
309725-04-0P 309725-05-1P 309725-07-3P 309725-10-8P
309725-12-0P 309725-14-2P 309725-16-4P 309725-18-6P
309725-20-0P 309725-28-8P 309725-32-4P 309725-34-6P
309725-36-8P 309728-22-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(oral A1 adenosine receptor agonists for treatment of tachycardia)

IT 79-09-4, Propionic acid, reactions 97-72-3, Isobutyric anhydride

103-82-2, Phenylethanoic acid, reactions 104-03-0, (4-Nitrophenyl)acetic acid 106-31-0, Butyric anhydride 108-24-7, Acetic anhydride 627-03-2, Ethoxyacetic acid 1149-26-4 2051-49-2, Hexanoic anhydride 3400-45-1, Cyclopentanecarboxylic acid 4530-20-5, N-Boc-glycine 20260-53-1, Nicotinoyl chloride hydrochloride 30379-55-6, Benzyloxyacetic acid 309725-29-9 309725-30-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(oral A1 adenosine receptor agonists for treatment of tachycardia)

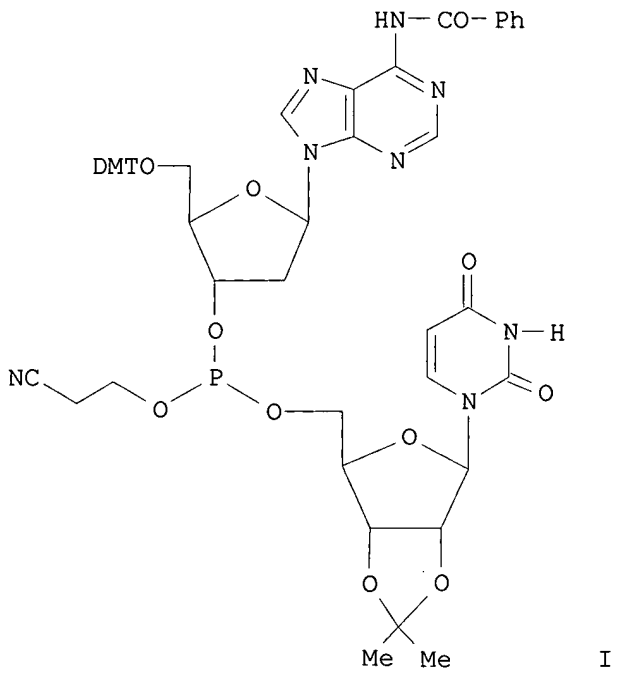
IT 309725-22-2P 309725-23-3P 309725-24-4P 309725-25-5P 309725-26-6P 309725-27-7P 309725-38-0P 309725-40-4P 309728-23-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(oral A1 adenosine receptor agonists for treatment of tachycardia)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 11 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:17686 MARPAT
TITLE: Oligonucleotide synthesis via coupling reaction with Lewis acids as activators
INVENTOR(S): Wang, Xiu C.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075157	A1	20001214	WO 2000-US12530	20000508
W: CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1181301	A1	20020227	EP 2000-926516	20000508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1999-325055 19990603
WO 2000-US12530 20000508
OTHER SOURCE(S): CASREACT 134:17686
GI



I

AB A process for synthesizing oligonucleotides by phosphoramidite chem. wherein the improvement is the use of Lewis acids as activators for formation of the phosphorous-oxygen bond. Thus, dimer oligodeoxyribonucleotide I was prepd. in quant. yield by Lewis acid-catalyzed coupling of nucleoside with nucleoside phosphoramidite.

IC ICM C07H019-04
ICS C07H021-00

CC 33-9 (Carbohydrates)

ST oligodeoxyribonucleotide synthesis Lewis acid catalyst coupling phosphoramidite

IT Coupling reaction
Coupling reaction catalysts
(oligonucleotide synthesis via coupling reaction with Lewis acids as activators)

IT Oligodeoxyribonucleotides
RL: SPN (Synthetic preparation); PREP (Preparation)
(oligonucleotide synthesis via coupling reaction with Lewis acids as activators)

IT 109-63-7, Borontrifluoride etherate 7446-70-0, Aluminum chloride (AlCl3), uses 7646-85-7, Zinc chloride (ZnCl2), uses 7699-45-8, Zinc bromide (ZnBr2) 7705-08-0, Iron(III) chloride, uses 7773-01-5, Manganese (II) chloride 7786-30-3, Magnesium chloride (MgCl2), uses 7787-60-2 7789-48-2, Magnesium bromide (MgBr2) 10026-11-6 60871-83-2, Magnesium triflate
RL: CAT (Catalyst use); USES (Uses)
(oligonucleotide synthesis via coupling reaction with Lewis acids as activators)

IT 362-43-6 98796-53-3
RL: RCT (Reactant); RACT (Reactant or reagent)

(oligonucleotide synthesis via coupling reaction with Lewis acids as activators)
IT 309972-12-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(oligonucleotide synthesis via coupling reaction with Lewis acids as activators)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

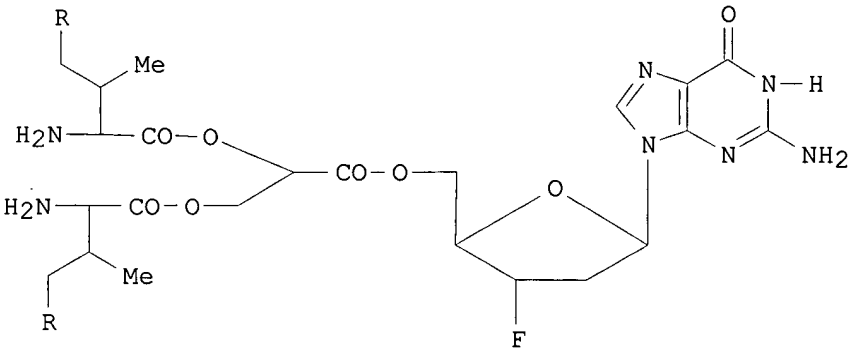
L17 ANSWER 12 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 131:144795 MARPAT
TITLE: Preparation of nucleosides as antiviral agents
INVENTOR(S): Wahling, Horst; Zhou, Xiao-xiong
PATENT ASSIGNEE(S): Medivir AB, Swed.
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9941268	A1	19990819	WO 1999-SE189	19990212
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 9909031	A1	19990225	WO 1998-SE1467	19980414
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9807267	A	19990215	ZA 1998-7267	19980813
EP 1123935	A2	20010816	EP 2001-103370	19980814
EP 1123935	A3	20010905		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
NZ 508502	A	20020426	NZ 1998-508502	19980814
ZA 9901148	A	19990812	ZA 1999-1148	19990212
CA 2318975	AA	19990819	CA 1999-2318975	19990212
EP 1058687	A1	20001213	EP 1999-932499	19990212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002503670	T2	20020205	JP 2000-531460	19990212
AU 9932819	A1	19990830	AU 1999-32819	19990830
AU 732408	B2	20010426		

PRIORITY APPLN. INFO.:

SE 1998-452	19980213
WO 1998-SE1467	19980414
ZA 1998-7267	19980813
SE 1997-2957	19970815
SE 1997-4147	19971112
EP 1998-939041	19980814
NZ 1998-502837	19980814
WO 1999-SE189	19990212

GI



I

AB Amino acid nucleosides I wherein R is independently H or CH3 were prepd. and are antivirally active against HBV and HIV. The prepn., formulation, and antiviral activity of 5'-O-[2,3-bis-(L-valyloxy)-propionyl]-2',3'-dideoxy-3'-fluoroguanosine were reported with significant enhancement of oral bioavailability.

IC ICM C07H019-16
ICS C07H019-167; A61K031-70; C07K005-00
CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 34
ST amino acid nucleoside prepn antiviral
IT Antiviral agents
Drug bioavailability
(prepn. of nucleosides as antiviral agents)
IT Amino acids, preparation
Nucleosides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of nucleosides as antiviral agents)
IT 235090-37-6P 235090-39-8P 235090-40-1P 235090-41-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of nucleosides as antiviral agents)
IT 1149-26-4 92562-88-4 235090-36-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of nucleosides as antiviral agents)
IT 235090-34-3P 235090-35-4P 235090-38-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT (Reactant or reagent)
(prepn. of nucleosides as antiviral agents)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 13 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:209924 MARPAT
TITLE: Preparation of amino acid-containing nucleoside esters as inhibitors of retroviral reverse transcriptase and hepatitis B virus DNA polymerase
INVENTOR(S): Zhou, Xiao-Xiong; Johansson, Nils-Gunnar; Wahling, Horst
PATENT ASSIGNEE(S): Medivir AB, Swed.
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9909031	A1	19990225	WO 1998-SE1467	19980414
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9887548	A1	19990308	AU 1998-87548	19980814
AU 728892	B2	20010118		
EP 988304	A1	20000329	EP 1998-939041	19980814
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
AT 200900	E	20010515	AT 1998-939041	19980814
EP 1123935	A2	20010816	EP 2001-103370	19980814
EP 1123935	A3	20010905		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
JP 2001515079	T2	20010918	JP 2000-509711	19980814
NZ 508502	A	20020426	NZ 1998-508502	19980814
ZA 9901148	A	19990812	ZA 1999-1148	19990212
CA 2318975	AA	19990819	CA 1999-2318975	19990212
WO 9941268	A1	19990819	WO 1999-SE189	19990212
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

EP 1058687	A1	20001213	EP 1999-932499	19990212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002503670	T2	20020205	JP 2000-531460	19990212
US 6458772	B1	20021001	US 1999-249317	19990212
CA 2318978	AA	19990819	CA 1999-2318978	19990215
WO 9941275	A1	19990819	WO 1999-SE194	19990215
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9932820	A1	19990830	AU 1999-32820	19990215
AU 754733	B2	20021121		
EP 1054891	A1	20001129	EP 1999-932500	19990215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002503673	T2	20020205	JP 2000-531466	19990215
CA 2325523	AA	19991014	CA 1999-2325523	19990330
WO 9951613	A1	19991014	WO 1999-SE528	19990330
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1121366	A1	20010808	EP 1999-921327	19990330
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002510698	T2	20020409	JP 2000-542334	19990330
AU 9932819	A1	19990830	AU 1999-32819	19990830
AU 732408	B2	20010426		
US 2002128301	A1	20020912	US 2001-927254	20010810
PRIORITY APPLN. INFO.:			SE 1997-2957	19970815
			SE 1997-4147	19971112
			SE 1998-452	19980213
			SE 1998-469	19980216
			SE 1998-1216	19980403
			WO 1998-SE1467	19980414
			ZA 1998-7267	19980813
			EP 1998-939041	19980814
			NZ 1998-502837	19980814
			SE 1998-3438	19981007
			US 1999-249317	19990212
			WO 1999-SE189	19990212
			WO 1999-SE194	19990215
			WO 1999-SE528	19990330
			WO 1999-SE1403	19990818

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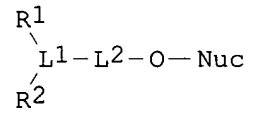

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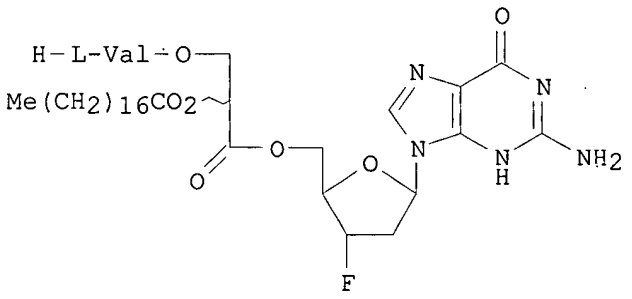


II

AB Nucleoside analogs I [Nuc = nucleoside analog residue bonded through its single hydroxy group on the cyclic or acyclic saccharide moiety; R1 = optionally esterified or amide bonded OH, NH2, CO2H, C4-C22 satd. or unsatd., optionally substituted fatty acid or alc., aliph. L-amino acid; R2 = aliph. L-amino acid residue; L1 = trifunctional linker group; L2 = bond, difunctional linker group] and pharmaceutically acceptable salts thereof have favorable pharmacol. properties and are antivirally active. Thus, nucleoside ester II was prepd. by esterification of 2',3'-dideoxy-3'-fluoroguanosine (FLG) with 3-(N-benzyloxycarbonyl-L-valyloxy)-2-stearoyloxypropanoic acid followed by hydrogenolysis. II showed 81.5% bioavailability of FLG after 6 h in a rat bioavailability assay model.

IC ICM C07D473-00
ICS C07D473-18; C07D473-32; C07H019-16; C07H019-167; C07H019-173; A61K031-52; A61K031-70

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 34, 63

ST nucleoside amino acid prodrug prepn virucide; hepatitis B virus inhibitor amino acid nucleoside ester prepn; DNA polymerase inhibitor amino acid nucleoside ester prepn; retroviral reverse transcriptase inhibitor amino acid nucleoside ester prepn

IT Nucleosides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid-contg. prodrugs; prepn. of amino acid-contg. nucleoside esters as inhibitors of retroviral reverse transcriptase and hepatitis B virus DNA polymerase)

IT Amino acids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(esters; prepn. of amino acid-contg. nucleoside esters as inhibitors of retroviral reverse transcriptase and hepatitis B virus DNA polymerase)

IT Antiviral agents

Hepatitis B virus
(prepn. of amino acid-contg. nucleoside esters as inhibitors of retroviral reverse transcriptase and hepatitis B virus DNA polymerase)

IT Drug delivery systems
(prodrugs; prepn. of amino acid-contg. nucleoside esters as inhibitors of retroviral reverse transcriptase and hepatitis B virus DNA polymerase)

IT 3056-17-5DP, d4T, amino acid-contg. prodrugs 7481-89-2DP, DdC, amino acid-contg. prodrugs 30516-87-1DP, AZT, amino acid-contg. prodrugs 59277-89-3DP, Acyclovir, amino acid-contg. prodrugs 69655-05-6DP, DdI, amino acid-contg. prodrugs 110143-10-7DP, F-DdA, amino acid-contg. prodrugs 134678-17-4DP, 3TC, amino acid-contg. prodrugs 136470-78-5DP, 1592U89, amino acid-contg. prodrugs 143491-54-7DP, FTC, amino acid-contg. prodrugs 145514-04-1DP, DAPD, amino acid-contg. prodrugs 220750-31-2P 220750-32-3P 220750-34-5P 220750-35-6P 220750-37-8P 220750-38-9P 220750-39-0P 220750-40-3P 220750-41-4P 220750-42-5P 220750-44-7P 220750-45-8P 220750-46-9P 220750-47-0P 220750-48-1P 220750-49-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid-contg. nucleoside esters as inhibitors of retroviral reverse transcriptase and hepatitis B virus DNA polymerase)

IT 9012-90-2D, DNA polymerase, hepatitis B virus
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(prepn. of amino acid-contg. nucleoside esters as inhibitors of retroviral reverse transcriptase and hepatitis B virus DNA polymerase)

IT 50-21-5, reactions 56-81-5, 1,2,3-Propanetriol, reactions 96-21-9, 1,3-Dibromo-2-propanol 105-13-5, 4-Methoxybenzyl alcohol 105-53-3, Diethyl malonate 108-30-5, Succinic anhydride, reactions 112-76-5, Stearoyl chloride 596-38-3, 9-Hydroxy-9-phenylxanthene 629-22-1, DL-2-Hydroxystearic acid 1149-26-4 2049-80-1, Diethyl allylmalonate 4767-03-7 6972-79-8, 1,3-Dibenzyloxy-2-propanol 15026-17-2 47522-06-5, N-Trityl-L-valine 50893-53-3, 1-Chloroethyl chloroformate 54555-84-9, 1-Benzyloxy-2-iodoethane 65644-56-6 68858-20-8 78385-36-1, (Benzyloxycarbonylmethyl)triphenylphosphonium bromide 92562-88-4 220750-88-9 220750-89-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of amino acid-contg. nucleoside esters as inhibitors of retroviral reverse transcriptase and hepatitis B virus DNA polymerase)

IT 123-94-4P 41478-45-9P 42201-43-4P, 2-Allyl-1,3-propanediol 42506-03-6P, Pixyl chloride 67065-61-6P 73573-57-6P 77661-80-4P 93132-52-6P 179388-73-9P 207973-06-6P 207973-07-7P 207973-08-8P 207973-09-9P 207973-10-2P 207973-11-3P 207973-12-4P 207973-13-5P 207973-14-6P 207973-15-7P 207973-16-8P 207973-17-9P 207973-18-0P 207973-21-5P 207973-22-6P 207973-23-7P 207973-24-8P 207973-25-9P 207973-26-0P 207973-27-1P 207973-28-2P 207973-29-3P 207973-31-7P 207973-33-9P 207973-36-2P 207973-38-4P 207973-41-9P 207973-43-1P 207973-44-2P 207973-45-3P 220750-25-4P 220750-26-5P 220750-28-7P

220750-29-8P 220750-30-1P 220750-33-4P 220750-36-7P
220750-50-5P 220750-52-7P 220750-53-8P 220750-54-9P
220750-55-0P 220750-56-1P 220750-57-2P 220750-58-3P
220750-59-4P 220750-60-7P 220750-61-8P 220750-62-9P
220750-63-0P 220750-64-1P 220750-65-2P 220750-67-4P
220750-68-5P 220750-69-6P 220750-70-9P 220750-71-0P
220750-72-1P 220750-73-2P 220750-74-3P 220750-75-4P
220750-76-5P 220750-77-6P 220750-78-7P 220750-79-8P
220750-80-1P 220750-81-2P 220750-82-3P 220750-83-4P
220750-85-6P 220750-86-7P 220750-87-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of amino acid-contg. nucleoside esters as inhibitors of retroviral reverse transcriptase and hepatitis B virus DNA polymerase)

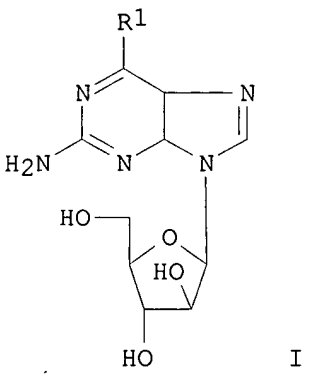
IT 9068-38-6, Reverse transcriptase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(retroviral; prepn. of amino acid-contg. nucleoside esters as inhibitors of retroviral reverse transcriptase and hepatitis B virus DNA polymerase)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 14 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 129:285982 MARPAT
TITLE: Method for treating B-cell tumors with ara-G nucleoside derivatives
INVENTOR(S): Averett, Devron Randolph; Koszalka, George Walter; Krenitsky, Thomas Anthony; McGuirt, Paul Vestal
PATENT ASSIGNEE(S): Glaxo Group Ltd., UK
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9842352	A1	19981001	WO 1998-US5771	19980323
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9867711	A1	19981020	AU 1998-67711	19980323
PRIORITY APPLN. INFO.:			US 1997-42352P	19970324
			GB 1997-6296	19970326
			WO 1998-US5771	19980323

GI



I

AB The invention relates to the treatment of B-cell lineage tumors (e.g. acute or chronic lymphocytic leukemias, acute or chronic myelogenous leukemias, or Hodgkin's or non Hodgkin's lymphomas) using arabinofuranosyl purine (ara-G) derivs. I (R1 = C1-5 alkoxy) or a pharmaceutically acceptable deriv. thereof (e.g. compds. esterified or derivatized on the sugar residue). These compds. can also be used in combination with a second therapeutic agent such as fludarabine for the same use(s).

IC ICM A61K031-70

CC 1-6 (Pharmacology)
Section cross-reference(s): 63

ST ara G deriv B cell tumor; fludarabine araG deriv B cell tumor

IT Antitumor agents
Antitumor agents
(B-cell lymphoma; ara-G nucleoside derivs. for B-cell tumor treatment)

IT Antitumor agents
Antitumor agents
(Hodgkin's disease inhibitors; ara-G nucleoside derivs. for B-cell tumor treatment)

IT Antitumor agents
Antitumor agents
(acute lymphocytic leukemia; ara-G nucleoside derivs. for B-cell tumor treatment)

IT Antitumor agents
(acute myelogenous leukemia; ara-G nucleoside derivs. for B-cell tumor treatment)

IT Drug delivery systems
(capsules, controlled-release; ara-G nucleoside derivs. for B-cell tumor treatment)

IT Drug delivery systems
(capsules; ara-G nucleoside derivs. for B-cell tumor treatment)

IT Antitumor agents
Antitumor agents
(chronic lymphocytic leukemia; ara-G nucleoside derivs. for B-cell tumor treatment)

IT Antitumor agents
(chronic myelocytic leukemia; ara-G nucleoside derivs. for B-cell tumor treatment)

IT Drug delivery systems
(freeze-dried; ara-G nucleoside derivs. for B-cell tumor

treatment)
IT Hodgkin's disease
Hodgkin's disease
(inhibitors; ara-G nucleoside derivs. for B-cell tumor treatment)
IT Drug delivery systems
(injections, i.m.; ara-G nucleoside derivs. for B-cell tumor treatment)
IT Drug delivery systems
(injections; ara-G nucleoside derivs. for B-cell tumor treatment)
IT Antitumor agents
(leukemia; ara-G nucleoside derivs. for B-cell tumor treatment)
IT Antitumor agents
(lymphoma; ara-G nucleoside derivs. for B-cell tumor treatment)
IT Antitumor agents
(myeloma; ara-G nucleoside derivs. for B-cell tumor treatment)
IT Antitumor agents
Antitumor agents
(non-Hodgkin's lymphoma; ara-G nucleoside derivs. for B-cell tumor treatment)
IT Drug delivery systems
(tablets, controlled-release; ara-G nucleoside derivs. for B-cell tumor treatment)
IT Drug delivery systems
(tablets; ara-G nucleoside derivs. for B-cell tumor treatment)
IT 38819-10-2D, derivs. 121032-29-9 141140-50-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ara-G nucleoside derivs. for B-cell tumor treatment)
IT 21679-14-1, Fludarabine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ara-G nucleoside derivs. with other agents for B-cell tumor treatment)
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 15 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 129:28180 MARPAT
TITLE: Preparation of amino acid-containing acyclic nucleoside esters as antiviral agents
INVENTOR(S): Zhou, Xiao-Xiong; Johansson, Nils-Gunnar
PATENT ASSIGNEE(S): Medivir AB, Swed.; Zhou, Xiao-Xiong; Johansson, Nils-Gunnar
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9821223	A1	19980522	WO 1997-SE1903	19971112

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP,

	KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU	735438	B2	19980603	AU 1999-50759	19971112
EP	942916	A2	19990922	EP 1997-913620	19971112
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP	2001503767	T2	20010321	JP 1998-522480	19971112
EP	1123935	A2	20010816	EP 2001-103370	19980814
EP	1123935	A3	20010905		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
NZ	508502	A	20020426	NZ 1998-508502	19980814
KR	2000053226	A	20000825	KR 1999-704201	19990512
PRIORITY APPLN. INFO.:				SE 1996-4154	19961112
				SE 1996-4165	19961112
				US 1997-798218	19970210
				SE 1997-2957	19970815
				US 1997-912927	19970815
				SE 1996-604165	19961112
				SE 1997-4147	19971112
				WO 1997-SE1903	19971112
				SE 1998-452	19980213
				EP 1998-939041	19980814
				NZ 1998-502837	19980814

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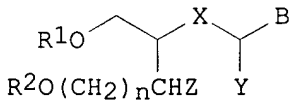


I

AB Mixed esters of antiviral nucleosides I, where B is natural or unnatural nucleotide base, X is O or CH2, Y and Z are each H, or together form a bond, or Y is methylene or -CH(OH)- and Z is a bond thereto; n is 0 or 1; one of R1 and R2 is the acyl residue of an aliph. amino acid and the other is -C(=O)C5-C21 satd. or mono-unsatd. alkyl; and pharmaceutically acceptable salts thereof have advantageous pharmacokinetics and other properties. Thus, 9-(4-stearoyloxy-3-(L-valyloxymethyl)butyl)guanine was prepd. and showed 22.7% bioavailability in rats.

IC ICM C07H019-06
ICS C07H019-067; C07H019-16; C07H019-167; C07D473-18; C07D473-32; C07D473-34; A61K031-52; A61K031-70

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 34, 63

ST acyclic nucleoside ester prepn antiviral

IT Amino acids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(nucleosides; prepn. of amino acid-contg. acyclic nucleoside esters as antiviral agents)

IT Antiviral agents
(prepn. of amino acid-contg. acyclic nucleoside esters as antiviral agents)

IT Nucleosides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid-contg. acyclic nucleoside esters as antiviral agents)

IT 107910-75-8P, Ganciclovir sodium 207972-89-2P 207972-91-6P 207972-93-8P 207972-96-1P 207972-98-3P 207973-00-0P 207973-01-1P 207973-03-3P 207973-06-6P 207973-52-2P 207973-54-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid-contg. acyclic nucleoside esters as antiviral agents)

IT 56-81-5, 1,2,3-Propanetriol, reactions 56-82-6, Glycerinaldehyde 112-76-5, Stearoyl chloride 147-94-4, AraC 596-38-3, 9-Hydroxy-9-phenylxanthene 1149-26-4 2049-80-1, Diethyl allylmalonate 4767-03-7 13139-16-7 13734-41-3 15761-38-3 32315-10-9, Bis(trichloromethyl)carbonate 36791-04-5 38819-10-2 39809-25-1 47522-06-5 68858-20-8 82410-32-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of amino acid-contg. acyclic nucleoside esters as antiviral agents)

IT 123-94-4P 42201-43-4P 42506-03-6P, Pixyl chloride 73573-57-6P 170935-63-4P 179388-73-9P 207972-87-0P 207972-88-1P 207972-90-5P 207972-92-7P 207972-94-9P 207972-95-0P 207972-97-2P 207972-99-4P 207973-02-2P 207973-04-4P 207973-05-5P 207973-07-7P 207973-08-8P 207973-09-9P 207973-10-2P 207973-11-3P 207973-12-4P 207973-13-5P 207973-14-6P 207973-15-7P 207973-16-8P 207973-17-9P 207973-18-0P 207973-21-5P 207973-22-6P 207973-23-7P 207973-24-8P 207973-25-9P 207973-26-0P 207973-27-1P 207973-28-2P 207973-29-3P 207973-31-7P 207973-33-9P 207973-36-2P 207973-38-4P 207973-41-9P 207973-43-1P 207973-44-2P 207973-45-3P 207973-46-4P 207973-47-5P 207973-49-7P 207973-50-0P 207973-53-3P 207973-55-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of amino acid-contg. acyclic nucleoside esters as antiviral agents)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 16 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 127:136038 MARPAT
TITLE: Reusable solid support for the oligodeoxyribonucleotide synthesis
INVENTOR(S): Pon, Richard T.; Yu, Shuyuan
PATENT ASSIGNEE(S): University Technologies International Inc.,

Can.; Pon, Richard T.; Yu, Shuyuan
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9723496	A1	19970703	WO 1996-CA836	19961213
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2241222	AA	19970703	CA 1996-2241222	19961213
CA 2241331	AA	19970703	CA 1996-2241331	19961213
AU 9710277	A1	19970717	AU 1997-10277	19961213
AU 725627	B2	20001019		
EP 876390	A1	19981111	EP 1996-940964	19961213
EP 876390	B1	20020612		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000502341	T2	20000229	JP 1997-523166	19961213
AT 219098	E	20020615	AT 1996-940964	19961213
US 6043353	A	20000328	US 1998-91527	19980619
PRIORITY APPLN. INFO.:			US 1995-9208P	19951222
			WO 1996-CA836	19961213

AB Linker arm solid support HORXCOYCOZQ [R = (un)substituted alkyl, aryl, alkaryl; X, Z = O, S, SO2 amine; Y = CH2CH2, CH2OCH2, CH:CH, CMe:CMe; CH2SCH2, CH2, CH2CH2CH2, CH:CMe, Q = solid support] was prepd. in synthesis of oligodeoxyribonucleotides. An aspect of the invention also relates to a linker arm for oligonucleotide synthesis based on the solid support. The linker arm is characterized by being reusable in an otherwise conventional oligonucleotide prodn. protocol.

IC ICM C07H021-00
CC 33-10 (Carbohydrates)
ST reusable solid support oligodeoxyribonucleotide synthesis; oxalyl succinyl linker solid support oligodeoxyribonucleotide; oligodeoxyribonucleotide solid phase prepn linker arm

IT Solid phase synthesis
(reusable solid support for the oligodeoxyribonucleotide synthesis)

IT Oligodeoxyribonucleotides
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(reusable solid support for the oligodeoxyribonucleotide synthesis)

IT 2245-53-6DP, Hydroquinone-O,O-diacetic acid, polymer support 109055-46-1DP, polymer support
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(reusable solid support for the oligodeoxyribonucleotide synthesis)

IT 151001-60-4P, PN: WO9946405 SEQID: 23 unclaimed DNA 193100-84-4P 193100-85-5P 193100-86-6P 193100-87-7P 193100-88-8P 193100-89-9P 193100-90-2P 193100-91-3P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

(Preparation)
(reusable solid support for the oligodeoxyribonucleotide synthesis)
IT 108-30-5, Succinic anhydride, reactions 616-47-7, N-Methylimidazole 2245-53-6, Hydroquinone-O,O-diacetic acid 2592-95-2 4048-33-3, 6-Amino-1-hexanol 39968-33-7 74405-40-6 74405-42-8 74405-44-0 94790-37-1, HBTU 148893-10-1, HATU
RL: RCT (Reactant); RACT (Reactant or reagent)
(reusable solid support for the oligodeoxyribonucleotide synthesis)

L17 ANSWER 17 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 127:109155 MARPAT
TITLE: Preparation of cholesterol conjugates of 2',5'-oligoadenylates as virucides
INVENTOR(S): Suhadolnik, Robert J.; Pfleiderer, Wolfgang
PATENT ASSIGNEE(S): Temple University-of the Commonwealth System of Pennsylvania, USA
SOURCE: U.S., 19 pp., Cont.-in-part of U.S. Ser. No. 849,865, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5643889	A	19970701	US 1994-306274	19940914
US 4859768	A	19890822	US 1988-144602	19880111
EP 716856	A2	19960619	EP 1996-101815	19890524
EP 716856	A3	19961030		
EP 716856	B1	20010829		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
IL 106709	A1	19961114	IL 1989-106709	19890601

PRIORITY APPLN. INFO.:

US 1984-629660	19840711
US 1988-144602	19880111
US 1988-204659	19880609
US 1990-613848	19901206
US 1992-849865	19920312
EP 1989-906575	19890524
IL 1989-90499	19890601

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = OCOR, OCO(CH2)xCOR, HO(PO3)m; n = 1-8; m= 1-3; x= 1-8; R2 = O, S; R3 = H, OH; R4, R5 = H, OH, OCOR, OCO(CH2)xCOR] were prepd. as virucides. The compds. possess increased antiviral activity and/or metabolic stability. Thus, 3'-deoxyadenylyl-(2'.fwdarw.5')-3'-deoxyadenylyl-(2'.fwdarw.5')-2'-O-[2(cholesteryloxycarbonyl)ethylcarbonyl]-3'-deoxyadenosine was prepd. and tested for its HIV-1 antiviral activity in peripheral blood lymphocytes (syncytia/plated cell = 1/200000) and (flow redn. in infection = 18000).

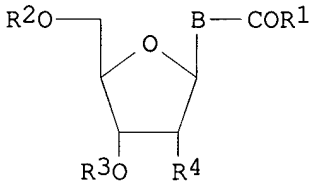
IC ICM A01G007-06
ICS A61K031-70
NCL 514044000
CC 33-10 (Carbohydrates)
Section cross-reference(s): 1, 32
ST oligodeoxyribonucleotide oligoadenylate cholesterol prepn virucide
IT Oligodeoxyribonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(cholesterol conjugates; prepn. of cholesterol conjugates of oligoadenylates as virucides)
IT Antiviral agents
(prepn. of cholesterol conjugates of oligoadenylates as virucides)
IT 162434-87-9P 162434-97-1P 192515-15-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of cholesterol conjugates of oligoadenylates as virucides)
IT 7144-08-3, Cholesteryl chloroformate 97776-92-6 97776-94-8 108787-34-4 156046-19-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of cholesterol conjugates of oligoadenylates as virucides)
IT 162434-74-4P 162434-75-5P 162434-76-6P 162434-77-7P
162434-78-8P 162434-80-2P 162434-81-3P 162434-82-4P
162434-83-5P 162434-84-6P 162434-85-7P 162434-86-8P
162434-88-0P 162434-89-1P 162434-90-4P 162434-91-5P
162434-92-6P 162434-93-7P 162434-94-8P 162434-95-9P
162434-96-0P 192515-13-2P 192515-14-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of cholesterol conjugates of oligoadenylates as virucides)
IT 162434-79-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of cholesterol conjugates of oligoadenylates as virucides)

L17 ANSWER 18 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:343815 MARPAT
TITLE: Synthesis of DNA using substituted phenylacetyl-protected nucleotides
INVENTOR(S): Reddy, M. Parameswara; Farooqui, Firdous; Hanna, Naeem B.
PATENT ASSIGNEE(S): Beckman Instruments, Inc., USA
SOURCE: U.S., 21 pp., Cont.-in-part of U.S. Ser. No. 207,433, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 5623068	A	19970422	US 1995-396993	19950301
WO 9524413	A1	19950914	WO 1995-US2831	19950307
W: JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 749436	A1	19961227	EP 1995-912770	19950307
R: DE, FR, GB				
JP 09510206	T2	19971014	JP 1995-523591	19950307
PRIORITY APPLN. INFO.:			US 1994-207433	19940307
			US 1995-396993	19950301
			WO 1995-US2831	19950307

GI



I

AB Nucleotides I (R1 = H, alkyl, aryl; R2, R3 = hydroxyl-protecting group; R4 = H, OH, protected OH; B = divalent radical corresponding to a purine or pyrimidine base) were prepd. in prepn. of DNA. When synthesis is carried out using these derivs., the deprotection procedure is reduced to an essentially instantaneous process. The derivs. have acceptable shelf life and are very stable to conventional DNA prepn. conditions. Thus, N2-(4-bromophenylacetyl)-5'-O-(4,4'-dimethoxytrityl)-2'-deoxyguanosine-3'-(N,N-diisopropyl)-methylphosphonamidite was prepd. in prepn. of DNA.

IC ICM C07H001-02
ICS C07H019-10; C07H019-20; C07H021-00

NCL 536025340

CC 33-10 (Carbohydrates)

ST nucleotide phenylacetyl protective group prepn DNA

IT Protective groups
(phenylacetyl; prepn. of DNA using substituted phenylacetyl-protected nucleotides)

IT DNA
RL: PNU (Preparation, unclassified); PREP (Preparation)
(prepn. of DNA using substituted phenylacetyl-protected nucleotides)

IT Nucleotides, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of DNA using substituted phenylacetyl-protected nucleotides)

IT 103-80-0, Phenylacetyl chloride 118-00-3, Guanosine, reactions 459-04-1, 4-Fluorophenylacetyl chloride 961-07-9, 2'-Deoxyguanosine 37859-24-8, 4-Bromophenylacetyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of DNA using substituted phenylacetyl-protected nucleotides)

IT 92447-25-1P 130150-80-0P 132628-16-1P 172965-87-6P 172965-89-8P 172965-91-2P 172965-92-3P 172965-93-4P

172965-94-5P 172965-95-6P 172965-96-7P 172965-97-8P
172965-99-0P 172966-00-6P 172966-04-0P 172966-05-1P
172966-06-2P 172966-07-3P 172966-08-4P 172966-17-5P
172966-19-7P 172966-20-0P 172966-21-1P 172966-23-3P
172966-24-4P 172966-25-5P 172966-26-6P 172966-27-7P
172966-28-8P 172966-29-9P 172966-30-2P 189745-30-0P
189745-32-2P 189745-45-7P 189745-58-2P 189745-60-6P
189745-62-8P 189745-64-0P 189745-65-1P 189745-67-3P
189745-69-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of DNA using substituted phenylacetyl-protected nucleotides)

L17 ANSWER 19 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:199797 MARPAT
TITLE: Preparation of carboranyl-contg. nucleosides for treatment of urogenital cancer with boron neutron capture therapy
INVENTOR(S): Schinazi, Raymond F.; Keane, Thomas E.; Liotta, Dennis C.
PATENT ASSIGNEE(S): Emory University, USA
SOURCE: U.S., 35 pp., Cont.-in-part of U.S. Ser. No. 161, 674.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5599796	A	19970204	US 1994-334759	19941104
US 6180766	B1	20010130	US 1993-161674	19931202
EP 1113020	A2	20010704	EP 2000-203565	19941202
R: BE, DE, ES, FR, GB, IT, SE				
ES 2161279	T3	20011201	ES 1995-904208	19941202
CA 2204160	AA	19960517	CA 1995-2204160	19951106
WO 9614073	A1	19960517	WO 1995-US14450	19951106
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9641483	A1	19960531	AU 1996-41483	19951106
AU 693618	B2	19980702		
EP 788364	A1	19970813	EP 1995-939803	19951106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10508603	T2	19980825	JP 1995-515485	19951106
US 5872107	A	19990216	US 1997-792370	19970203
US 2002160969	A1	20021031	US 2001-774223	20010130
PRIORITY APPLN. INFO.:			US 1993-161674	19931202
			US 1994-334759	19941104
			EP 1995-904208	19941202
			WO 1995-US14450	19951106

AB Methods and compns. for treating urogenital tumors, and particular, cancer of the prostate, bladder, and kidney, with BCNT, are disclosed. Any boron-contg. nucleoside that is sufficiently lipophilic to pass through the appropriate urogenital membranes in a

quantity high enough to achieve therapy on irradn. with low-energy neutrons can be used. Carboranyl-contg. nucleosides and oligonucleotides are particularly suited for use in BNCT of urogenital tumors. Preferred compds. include 5-carboranyl-2'-deoxyuridine (CDU) and 5-o-carboranyl-1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)uracil (CFAU). Nucleosides and oligonucleotides bearing an -O-[(carboran-1-yl)alkyl]phosphate, S-[(carboran-1-yl)alkyl]phosphorothioate, or Se-[(carboran-1-yl)alkyl]phosphoroselenoate in place of the (carboran-1-yl)phosphonate moiety can be used. Oligonucleotides of specific gene sequences that include one or more 3',5'-linking-(carboran-1-yl)phosphonate moieties can also be used in antisense therapy in the selective modification of gene expression. The therapy is accomplished by administering the boron-contg. compd. by any appropriate route, including by i.v. injection, oral delivery or by catheter or other direct means, in such a manner that the compd. accumulates in the target tumor. After desired accumulation of the compd. in the tumor, the site is irradiated with an effective amt. of low energy neutrons.

IC ICM A61K031-69
ICS A61K041-00; A61K043-00

NCL 514044000

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 63

ST carboranyldeoxyfluoroarabinouracil prepn antitumor urogenital; boron neutron capture therapy nucleoside prepn; carboranyldeoxyuridine prepn antitumor urogenital; carboranyl nucleoside prepn antitumor urogenital

IT Radiotherapy
(boron-neutron capture; prepn. of carboranyl-contg. nucleosides for treatment of urogenital cancer with boron neutron capture therapy)

IT Nucleosides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(carboranyl-contg.; prepn. of carboranyl-contg. nucleosides for treatment of urogenital cancer with boron neutron capture therapy)

IT Antitumor agents
(urogenital; prepn. of carboranyl-contg. nucleosides for treatment of urogenital cancer with boron neutron capture therapy)

IT 140424-79-9P 140424-80-2P 157444-53-6P 178763-35-4P 187891-84-5DP, tritiated
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of carboranyl-contg. nucleosides for treatment of urogenital cancer with boron neutron capture therapy)

IT 106-96-7, Propargyl bromide 17702-41-9, Decaborane 21090-30-2, 3'-O-Acetylthymidine 53176-11-7, Triisopropylbenzenesulfonyl chloride 69123-98-4 143446-73-5 157444-56-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of carboranyl-contg. nucleosides for treatment of urogenital cancer with boron neutron capture therapy)

IT 52522-99-3P 59989-18-3P 83355-88-8P 83355-89-9P 83355-90-2P
133368-76-0P 140424-78-8P 151204-22-7P 151545-30-1P
151545-32-3P 151545-33-4P 151545-35-6P 151545-36-7P
151545-37-8P 151594-04-6P 151636-26-9P 157428-24-5P
157444-55-8P 159068-20-9P 159068-21-0P 171796-50-2P
171796-51-3P 178763-38-7P 178763-40-1P 178763-41-2P
178763-43-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of carboranyl-contg. nucleosides for treatment of urogenital cancer with boron neutron capture therapy)

IT 4885-44-3P 151204-23-8P 157428-25-6P 178763-36-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of carboranyl-contg. nucleosides for treatment of urogenital cancer with boron neutron capture therapy)

L17 ANSWER 20 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 125:115081 MARPAT
TITLE: Solid phase synthesis of oligonucleotides with stereospecific substituted phosphonate linkages by pentavalent Grignard coupling.
INVENTOR(S): Wickstrom, Eric; Le Bec, Christine
PATENT ASSIGNEE(S): Thomas Jefferson University, USA
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9607663	A1	19960314	WO 1995-US10866	19950828
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5703223	A	19971230	US 1994-300259	19940902
PRIORITY APPLN. INFO.:			US 1994-300259	19940902

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds., e.g., [I, II; Y1 = H, V1; Y2 = H, V2; B = (substituted) purine, pyrimidine base; Z1, Z2 = H, OH, OY3; Y3 = (substituted) alkyl; M = alkyl, aryl, borano, amino; V1 = nonporous solid support; V2 = protecting group], were prepd. by treatment of 5'-deprotected nucleosides (III or IV; variables as above) with RMgX [R = (substituted) alkyl, allyl, aralkyl, aryl; X = halo] and coupling the product with 5'-protected nucleotides (V, VI; L = leaving group; other variables as above) under conditions sufficient to produce a stereospecifically substituted phosphonate linkages. The method can be used for automated synthesis of oligonucleotides having sequential equatorial or axial stereospecific substituted phosphonate linkages. Thus, N2-isobutyryl-3'-O-succinyl-2'-deoxyguanosine supported on high-loaded polystyrene beads

derivatized with aminoethylpolyethylene glycol monomethyl ether (HLP) (prepn. given) in pyridine was treated with Me3CMgBr and then with Eq-5'-O-dimethoxytrityl-N4-benzoyl-2'-deoxyadenosine-3'-O-(4-nitrophenyl)methylphosphonate to give Ax-5'-O-dimethoxytrityl-N4-benzoyl-2'-deoxyadenosine-3'-O-methylphosphonate-2'-deoxyadenylyl-N2-isobutyryl-3'-O-succinyl-2-deoxguanosine-HLP.

IC ICM C07H001-02
ICS C07H021-00; C07H021-04

CC 33-9 (Carbohydrates)

ST oligonucleotide stereospecific substituted phosphonate linkage prepn; grignard coupling stereospecific nucleotide nucleoside

IT Nucleotides, preparation
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(oligo-, solid phase synthesis of oligonucleotides with stereospecific substituted phosphonate linkages by pentavalent Grignard coupling)

IT Synthesis
(stereoselective, solid phase synthesis of oligonucleotides with stereospecific substituted phosphonate linkages by pentavalent Grignard coupling)

IT 161522-97-0P 161597-35-9P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(solid phase synthesis of oligonucleotides with stereospecific substituted phosphonate linkages by pentavalent Grignard coupling)

IT 161522-98-1P 161597-36-0P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(solid phase synthesis of oligonucleotides with stereospecific substituted phosphonate linkages by pentavalent Grignard coupling)

IT 100-02-7, 4-Nitrophenol, reactions 108-30-5, Succinic anhydride, reactions 676-97-1, Methylphosphonic dichloride 677-22-5, tert-Butylmagnesium chloride 9004-74-4, Polyethylene glycol monomethyl ether 64325-78-6, 5'-O-Dimethoxytrityl-N6-benzoyl-2'-deoxyadenosine 81144-43-6, 5'-O-Dimethoxytrityl-2'-deoxyguanosine 129904-67-2, 5'-O-Dimethoxytrityl-N4-isobutyryl-2'-deoxycytidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid phase synthesis of oligonucleotides with stereospecific substituted phosphonate linkages by pentavalent Grignard coupling)

IT 74405-46-2DP, polymer support 74405-46-2P 95262-44-5DP, polymer support 95262-44-5DP, resin-bound 161522-95-8P 161522-96-9P 161597-35-9DP, resin-bound 178871-79-9P 178871-80-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(solid phase synthesis of oligonucleotides with stereospecific substituted phosphonate linkages by pentavalent Grignard coupling)

L17 ANSWER 21 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 125:96065 MARPAT
TITLE: Ether lipid-nucleoside covalent conjugates
INVENTOR(S): Piantadosi, Claude; Marasco, Canio J., Jr.; Kucera, Louis S.
PATENT ASSIGNEE(S): Wake Forest University, USA; University of North

Carolina
SOURCE: U.S., 11 pp., Cont. of U. S. Ser. No. 955, 709, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5512671	A	19960430	US 1995-418853	19950407
PRIORITY APPLN. INFO.:			US 1993-955709	19930216

AB Conjugates of ether lipids and antiviral nucleoside analogs are disclosed, along with pharmaceutical compns. contg. the same and methods of using the same to combat HIV-1 infections. Illustrative are 3'-azido-3'-deoxythymidine-5'-monophosphatoxypropane and 3'-azido-3'-deoxythymidine-5'-butyrate-.gamma.-N,N,N-trimethyammonium-.beta.-(1-phospho-2-ethoxy-3-hexadecyloxypropane).

IC ICM C07H019-20
NCL 536026100
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 23, 33
ST phospholipid nucleoside conjugate virucide HIV1 virus

IT Virucides and Virustats
(phospholipid-nucleoside conjugates as virucides for treatment of HIV-1 infections)

IT Phospholipids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates, ether-linked, with nucleoside analogs; phospholipid-nucleoside conjugates as virucides for treatment of HIV-1 infections)

IT Nucleosides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates, with phospholipids; phospholipid-nucleoside conjugates as virucides for treatment of HIV-1 infections)

IT Phospholipids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ether-linked, conjugates with nucleoside analogs; phospholipid-nucleoside conjugates as virucides for treatment of HIV-1 infections)

IT Virus, animal
(human immunodeficiency 1, phospholipid-nucleoside conjugates as virucides for treatment of HIV-1 infections)

IT 139964-27-5P 139964-28-6P 139964-29-7P 139964-30-0P
139964-32-2P 139964-40-2P 139964-41-3P 178393-96-9P
178393-97-0P 178393-98-1P 178393-99-2P 178394-00-8P
178394-01-9P 178394-02-0P 178394-03-1P 178394-04-2P
178394-05-3P 178394-06-4P 178394-07-5P 178394-08-6P

178394-09-7P 178394-10-0P 178394-11-1P 178394-12-2P
178394-13-3P 178394-14-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phospholipid-nucleoside conjugates as virucides for treatment of HIV-1 infections)

IT 2524-64-3, Diphenylchlorophosphate 30516-87-1, AZT 69655-05-6, DDI 106060-91-7 113760-82-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(phospholipid-nucleoside conjugates as virucides for treatment of HIV-1 infections)

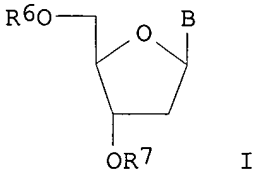
IT 139964-34-4P 139964-35-5P 139964-37-7P 139964-38-8P
178394-15-5P 178394-16-6P 178394-17-7P 178394-18-8P
178394-19-9P 178394-20-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(phospholipid-nucleoside conjugates as virucides for treatment of HIV-1 infections)

L17 ANSWER 22 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 125:87106 MARPAT
TITLE: Preparation of activated nucleoside phosphoramidites for oligonucleotide synthesis.
INVENTOR(S): Reddy, M. Parameswara; Farooqui, Firdous
PATENT ASSIGNEE(S): Beckman Instruments, Inc., USA
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9606853	A1	19960307	WO 1995-US10609	19950818
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5574146	A	19961112	US 1994-298545	19940830
CA 2174216	AA	19960317	CA 1995-2174216	19950818
AU 9533692	A1	19960322	AU 1995-33692	19950818
AU 688577	B2	19980312		
EP 725787	A1	19960814	EP 1995-930233	19950818
R: DE, FR, GB				
JP 09504805	T2	19970513	JP 1995-508818	19950818

PRIORITY APPLN. INFO.: US 1994-298545 19940830
WO 1995-US10609 19950818

GI



I

AB Title compds. (I; 1 of R6, R7 = R3, the other = P(R2)OR1; R1 = substituted arylcarbonyl group; R2 = R4O, R5; R3 = protecting group; and B = purine or pyrimidine base; R4, R5 undefined), were prepd. in situ. Particularly preferred are those compds. wherein R1 = 2,4-dinitrophenylcarbonyl. I may be employed in conventional coupling reactions (e.g., solid phase synthesis) to prep. oligonucleotides which are indistinguishable from those prepd. using tetrazole-activated nucleoside intermediates. 2,4-Dinitrobenzoic acid was used in solid phase phosphoramidite synthesis of oligonucleotides, oligonucleoside methylphosphonates, and oligonucleotide phosphorothioates with coupling efficiencies of 97-99%.

IC ICM C07H019-10
ICS C07H019-20; C07H021-00; C07H021-04

CC 33-9 (Carbohydrates)

ST oligonucleotide synthesis activator arylcarboxylate

IT Nucleotides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(oligo-, prepn. by phosphoramidite chem. using arylcarboxylate activators)

IT 610-30-0, 2,4-Dinitrobenzoic acid 98796-51-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of activated nucleoside phosphoramidites)

IT 158653-50-0P 178537-91-2P 178537-92-3P 178537-93-4P 178537-94-5P 178537-95-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis using 2,4-dinitrobenzoic acid activator; prepn. of activated nucleoside phosphoramidites)

L17 ANSWER 23 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 125:80778 MARPAT
TITLE: Treatment of urogenital cancer with boron neutron capture therapy, and preparation of carboranyl-containing nucleosides and nucleotides
INVENTOR(S): Schinazi, Raymond F.; Keane, Thomas E.; Liotta, Dennis C.
PATENT ASSIGNEE(S): Emory University, USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9614073	A1	19960517	WO 1995-US14450	19951106

	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5599796		A	19970204	US 1994-334759	19941104
AU 9641483		A1	19960531	AU 1996-41483	19951106
AU 693618		B2	19980702		
EP 788364		A1	19970813	EP 1995-939803	19951106
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10508603		T2	19980825	JP 1995-515485	19951106
PRIORITY APPLN. INFO.:				US 1994-334759	19941104
				US 1993-161674	19931202
				WO 1995-US14450	19951106

AB Methods and compns. for treating urogenital tumors, and in particular, cancer of the prostate, bladder, and kidney, with boron neutron capture therapy (BNCT), are disclosed. Any boron-contg. compd. that is sufficiently lipophilic to pass through the appropriate urogenital membranes in a quantity high enough to achieve therapy on irradn. with low-energy neutrons can be used. Carboranyl-contg. nucleosides and oligonucleotides are particularly suited for use in BNCT of urogenital tumors. Preferred compds. include 5-carboranyl-2'-deoxyuridine (CDU) and 5-O-carboranyl-1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)uracil (CFAU). Nucleosides and oligonucleotides bearing an -O-[(carboran-1-yl)alkyl]phosphate, S-[(carboran-1-yl)alkyl]phosphorothioate, or Se-[(carboran-1-yl)alkyl]phosphoroselenoate in place of the (carboran-1-yl)phosphonate moiety can be used. Oligonucleotides of specific gene sequences that include one or more 3', 5'-linking-(carboran-1-yl)phosphonate moieties can also be used in antisense therapy in the selective modification of gene expression. Compds. can be used in urogenital BNCT therapy that contain boron clusters as a means to enhance lipophilicity wherein the boron is not enriched in 10B, but instead, in the 11B isotope. The therapy is accomplished by administering the boron-contg. compd. by any appropriate route, including by i.v. injection, oral delivery or by catheter or other direct means, in such a manner that the compd. accumulates in the target tumor. After desired accumulation of the compd. in the tumor, the site is irradiated with an effective amt. of low energy neutrons. In in vivo studies with human prostate tumor xenograft-bearing nude mice, CDU showed significant blood levels after i.p. injection of radiolabeled compd. At 2 h after treatment, the level of drug localized in the tumor (s.c. xenograft) was 11-fold greater than in normal tissue (brain) and 2- to 3-fold higher than in serum. Prepn. of CFAU and other compds. is described.

IC ICM A61K031-69
ICS A61K031-70

CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 29, 33

ST boron neutron capture therapy urogenital tumor; carboranyl nucleoside prepn neutron capture therapy; nucleotide carboranyl prepn neutron capture therapy; antisense therapy boron neutron capture urogenital

IT Nucleosides, biological studies
Nucleotides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)

IT Neoplasm inhibitors
(bladder carcinoma, urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)
IT Radiotherapy
(boron-neutron capture, urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)
IT Neoplasm inhibitors
(genitourinary tract, urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)
IT Kidney, neoplasm
(inhibitors, urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)
IT Neoplasm inhibitors
(kidney, urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)
IT Proteins, specific or class, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ligand-binding, 5-carboranyl-2'-deoxyuridine pharmacokinetics and protein binding)
IT Bladder
(neoplasm, carcinoma, inhibitors, urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)
IT Genitourinary tract
Prostate gland
(neoplasm, inhibitors, urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)
IT Nucleotides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oligo-, and antisense oligonucleotides; urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)
IT Neoplasm inhibitors
(prostate gland, urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)
IT Ribonucleic acid formation factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(repressors, boron-10-contg. antisense oligonucleotide deriv. suppressing biosynthesis of; urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)
IT 140424-79-9
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)
IT 157444-53-6P
RL: ADV (Adverse effect, including toxicity); SPN (Synthetic

preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)

IT 93-97-0, Benzoic anhydride 98-88-4, Benzoyl chloride 100-44-7, Benzyl chloride, reactions 106-96-7, Propargyl bromide 108-24-7, Acetic anhydride 121-44-8, reactions 121-45-9, Trimethylphosphite 999-97-3, 1,1,1,3,3,3-Hexamethyldisilazane 1066-54-2, (Trimethylsilyl)acetylene 6974-32-9 17702-41-9, Decaborane 21090-30-2, 3'-O-Acetylthymidine 23094-61-3 42926-80-7 69123-98-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)

IT 4885-44-3P 59989-18-3P, 5-Ethynyluracil 83355-88-8P 133368-76-0P 151545-30-1P 151545-32-3P 151545-35-6P 151545-36-7P 151636-26-9P 159068-21-0P 171796-50-2P 171796-51-3P 171962-13-3P 171962-14-4P 178763-37-6P 178763-38-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)

IT 157444-55-8P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)

IT 52522-99-3P, 2,4-Dimethoxy-5-iodopyrimidine 62803-27-4P 83355-90-2P 151204-22-7P 151545-37-8P 151594-04-6P 157428-25-6P 159068-20-9P 178763-36-5P 178763-40-1P 178763-41-2P 178763-42-3P 178763-43-4P 178763-44-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)

IT 51-21-8D, 5-Fluorouracil, boron-10-contg. derivs. 65-71-4D, Thymine, boron-10-contg. derivs. 66-22-8D, Uracil, boron-10-contg. derivs. 71-30-7D, Cytosine, boron-10-contg. derivs. 73-24-5D, Adenine, boron-10-contg. derivs. 73-40-5D, Guanine, boron-10-contg. derivs. 87-42-3D, 6-Chloropurine, boron-10-contg. derivs. 120-73-0D, Purine, carboranyl derivs. 141-90-2D, 2-Thiouracil, boron-10-contg. derivs. 289-95-2D, Pyrimidine, carboranyl derivs. 452-06-2D, 2-Aminopurine, boron-10-contg. derivs. 591-28-6D, 4-Thiouracil, boron-10-contg. derivs. 1904-98-9D, 2,6-Diaminopurine, boron-10-contg. derivs. 2001-93-6D, 2,4(1H,3H)-Pyrimidinedithione, boron-10-contg. derivs. 2022-85-7D, 5-Fluorocytosine, boron-10-contg. derivs. 10310-21-1D, 2-Amino-6-chloropurine, boron-10-contg. derivs. 14798-12-0D, Boron-10, compds. contg., biological studies 140424-78-8 140424-80-2 151204-23-8 178763-35-4 178763-39-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(urogenital cancer treatment with boron neutron capture therapy, and prepn. of carboranyl-contg. nucleosides and nucleotides)

L17 ANSWER 24 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 124:317783 MARPAT
TITLE: Preparation of nucleosides and antisense

	oligonucleotides containing boron clusters for use in boron neutron capture therapy (BNCT) of cancer
INVENTOR(S):	Schinazi, Raymond F.; Kattan, Geraldine F.; Lesnikowski, Zbigniew J.
PATENT ASSIGNEE(S):	Emory University, USA
SOURCE:	PCT Int. Appl., 108 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9515333	A1	19950608	WO 1994-US13835	19941202
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6180766	B1	20010130	US 1993-161674	19931202
AU 9512991	A1	19950619	AU 1995-12991	19941202
AU 685892	B2	19980129		
EP 731808	A1	19960918	EP 1995-904208	19941202
EP 731808	B1	20010711		
R: BE, DE, ES, FR, GB, IT, SE				
JP 10505318	T2	19980526	JP 1994-515775	19941202
EP 1113020	A2	20010704	EP 2000-203565	19941202
R: BE, DE, ES, FR, GB, IT, SE				
ES 2161279	T3	20011201	ES 1995-904208	19941202
US 2002160969	A1	20021031	US 2001-774223	20010130
PRIORITY APPLN. INFO.:			US 1993-161674	19931202
			EP 1995-904208	19941202
			WO 1994-US13835	19941202

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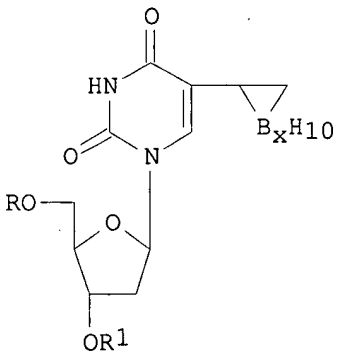

I

AB Carboranyl-contg. nucleosides and oligonucleotides, which contain at least one uncharged 3',5'-O,O-[(carboran-1-ylmethyl)phosphonate] internucleotide linkage or at least one carboranyl-contg. base and are capable of hybridization in vivo to a complimentary DNA nucleic acid sequence or to a specific gene sequence in double stranded DNA to form a triple stranded complex, are prepd. These

carboranyl-contg. oligonucleotides are used as (1) radiosensitizers for boron neutron capture therapy of tumors, (2) antisense agents for inducing a mutation during transcription or cell division in a viral genome (in particular HIV and HBV) or eukaryotic or procaryotic genome by hybridization to a nucleic acid sequence, (3) magnetic resonance imaging (MRI) probes for detecting the presence or location of tumors in a patient using MRI by selectively accumulating the oligonucleotides in the tumor tissue, or (4) nucleic acid hybridization probes for detecting a target nucleic acid sequence by hybridization of the oligonucleotides to the target sequence and detecting the hybrid. Thus, 5-(o-carboran-1-yl)-2'-O-deoxyuridine (I; R = R1 = H; x = 9 or 10) was alkylated by 4,4'-dimethoxytrityl chloride in pyridine to give I (R = 4,4'-dimethoxytrityl, R1 = H; x = 9 or 10) which was condensed with 2-cyanoethyl-N,N-diisopropylaminophosphine in the presence of diisopropylethylamine in CH2Cl2 to give a 3'-phosphoramidite I [R = 4,4'-dimethoxytrityl, R1 = P(CH2CH2CN)N(CHMe2)2; x = 9 or 10]. The phosphoramidite was incorporated into oligonucleotides, e.g. 5'-AATACATGGA(CDU)GATTTGTAT-3' [CDU = 5-(o-carboran-1-yl)-2'-O-deoxyuridine residue] (II) and 5'-AATACATGG(CDU)2GATTTGTAT-3' (III) by automated synthesis using an Applied Biosystems 391 DNA synthesizer. Oligonucleotides II and III in vitro showed site directed mutagenesis on pHIVALT-1 ssDNA.

IC ICM C07H021-00
ICS C07H021-02; C07H021-04; C07H023-00; A61K031-00; A61K031-69; A61K048-00; A61K049-00

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1

ST antisense oligonucleotide contg boron cluster prepn; HIV antisense carborane contg oligonucleotide; HBV antisense carborane contg oligonucleotide; boron neutron capture therapy cancer; magnetic resonance imaging probe; nucleic acid hybridization probe

IT Nucleic acid hybridization
(prepn. of antisense oligonucleotides contg. boron clusters as probes for magnetic resonance imaging of tumor and nucleic acid hybridization)

IT Virucides and Virustats
(prepn. of antisense oligonucleotides contg. boron clusters as radiosensitizers in boron neutron capture therapy of cancer and as antiviral agents for HIV and HBV)

IT Neoplasm inhibitors
Radiosensitizers, biological
(prepn. of antisense oligonucleotides contg. boron clusters as radiosensitizers in boron neutron capture therapy of cancer and as probes for magnetic resonance imaging of tumor)

IT Imaging
(NMR, prepn. of antisense oligonucleotides contg. boron clusters as radiosensitizers in boron neutron capture therapy of cancer and as probes for magnetic resonance imaging of tumor)

IT Radiotherapy
(neutron capture, prepn. of antisense oligonucleotides contg. boron clusters as radiosensitizers in boron neutron capture therapy of cancer and as probes for magnetic resonance imaging of tumor)

IT Nucleotides, preparation
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(oligo-, prepn. of antisense oligonucleotides contg. boron clusters as radiosensitizers in boron neutron capture therapy of cancer and as probes for magnetic resonance imaging of tumor)

IT 151545-37-8P 151594-04-6P 164641-32-1P 164641-33-2P
164641-34-3P 166943-40-4P 166943-42-6P 166943-44-8P
166943-46-0P 166943-47-1P 166943-48-2P 175959-90-7P
175959-91-8P 175959-92-9P 175960-98-2P 175960-99-3P
175961-00-9P 175961-01-0P 175961-02-1P 175961-03-2P
175961-04-3P 175961-05-4P 175961-06-5P 175961-07-6P
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of antisense oligonucleotides contg. boron clusters as radiosensitizers in boron neutron capture therapy of cancer and as probes for magnetic resonance imaging of tumor)

IT 54-42-2, 5-Iodo-2'-deoxyuridine 106-96-7, Propargyl bromide
121-45-9, Trimethyl phosphite 17702-41-9, Decaborane 21090-30-2,
3'-O-Acetylthymidine 40615-36-9, 4,4'-Dimethoxytrityl chloride
42926-80-7 89992-70-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of antisense oligonucleotides contg. boron clusters as radiosensitizers in boron neutron capture therapy of cancer and as probes for magnetic resonance imaging of tumor)

IT 4885-44-3P, Dimethyl propargylphosphonate 140424-79-9P
151545-30-1P 151545-32-3P 151545-35-6P 151545-36-7P
151636-26-9P 161651-50-9P 161697-64-9P 171783-87-2P
171783-88-3P 171783-89-4P 171796-50-2P 171796-51-3P
171962-13-3P 171962-14-4P 171962-15-5P 171962-16-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of antisense oligonucleotides contg. boron clusters as radiosensitizers in boron neutron capture therapy of cancer and as probes for magnetic resonance imaging of tumor)

L17 ANSWER 25 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 124:117892 MARPAT
TITLE: Compositions and methods using a phenylacetyl protecting group for use in the synthesis of oligonucleotides
INVENTOR(S): Reddy, Meda Parameswara; Hanna, Naeem B.; Farooqui, Firdous
PATENT ASSIGNEE(S): Beckman Instruments, Inc., USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9524413	A1	19950914	WO 1995-US2831	19950307
W: JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5623068	A	19970422	US 1995-396993	19950301
EP 749436	A1	19961227	EP 1995-912770	19950307
R: DE, FR, GB				

JP 09510206 T2 19971014 JP 1995-523591 19950307
PRIORITY APPLN. INFO.: US 1994-207433 19940307
US 1995-396993 19950301
WO 1995-US2831 19950307
OTHER SOURCE(S): CASREACT 124:117892
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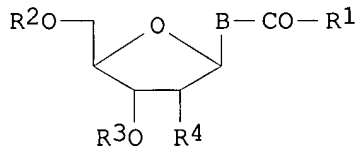

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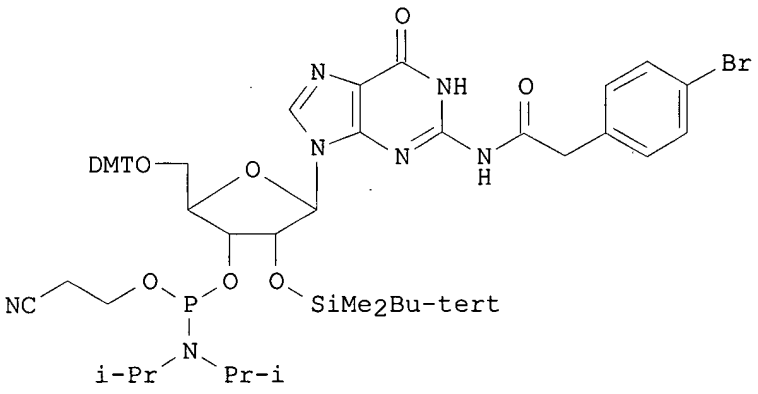


II

AB Phenylacetyl-protected deoxyribonucleotide and ribonucleotide derivs. are claimed, specifically I [R1 = CR'R''Ar; Ar = (un)substituted aryl; R', R'' = H, alkyl; 1 of R2 and R3 = OH-protecting group, other = group suitable for synthesis of polynucleotides or for attachment of the nucleoside to a solid support; R4 = H, OH, protected OH; B = divalent radical corresponding to purine or pyrimidine base]. When synthesis is carried out using these derivs., the deprotection procedure is reduced to an essentially instantaneous process. The derivs. have acceptable shelf life and are very stable to conventional DNA synthesis conditions. Particularly preferred are I wherein Ar is mono- and dihalo-substituted Ph. For example, guanosine underwent silylation, acylation with 4-BrC6H4CH2COCl, and deprotection to give 60% of the N2-(4-bromophenylacetyl) deriv., which was 5'-O-tritylated with 4,4'-dimethoxytrityl chloride (50%). This underwent 2'-O-silylation (13%) and reaction with NCCH2CH2PClN(Pr-iso)2 (50%) to give title compd. II. An oligonucleotide derivable from II was deprotected by MeNH2 in 7 min at 25.degree., whereas a conventional iso-Bu protecting group required 60 min. Similar deprotections of other I-derived oligonucleotides with MeNH2 required < 30 s at 65.degree..

IC ICM C07H019-06
ICS C07H019-16
CC 33-9 (Carbohydrates)

ST phenylacetyl protecting group nucleotide; oligonucleotide prepn
phenylacetyl protecting group

IT Aminolysis
Kinetics of aminolysis
(prepn. of arylacetyl-protected nucleotide derivs. for prepn. of oligonucleotides)

IT Deoxyribonucleic acids
Ribonucleic acids
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of arylacetyl-protected nucleotide derivs. for prepn. of oligonucleotides)

IT Nucleotides, preparation
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(oligo-, prepn. of arylacetyl-protected nucleotide derivs. for prepn. of oligonucleotides)

IT 74-89-5, Methanamine, reactions 1336-21-6, Ammonium hydroxide 7664-41-7, Ammonia, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(deprotecting agent; prepn. of arylacetyl-protected nucleotide derivs. for prepn. of oligonucleotides)

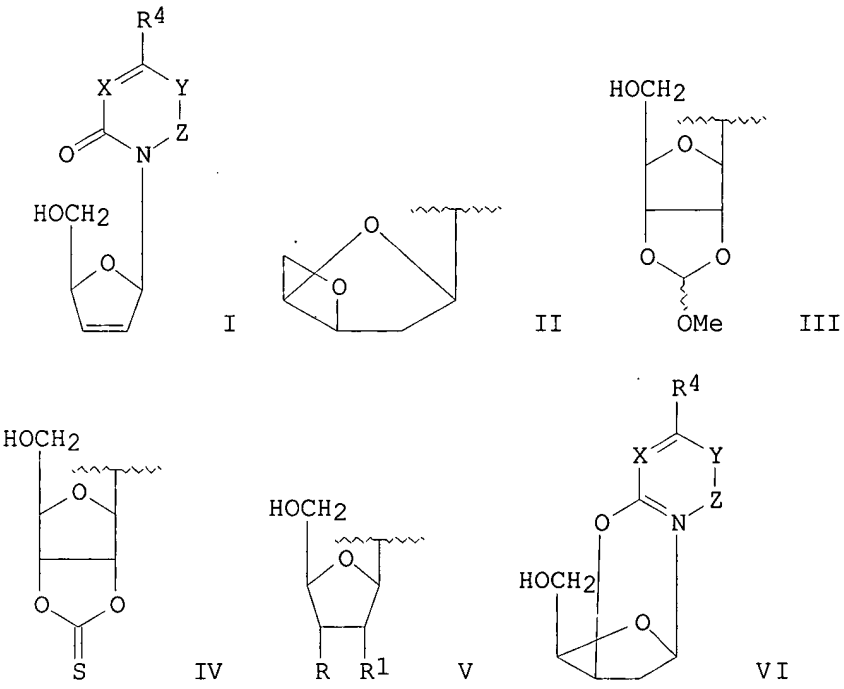
IT 132628-16-1DP, oligonucleotide deriv. 172966-24-4DP, oligonucleotide deriv. 172966-25-5DP, oligonucleotide deriv. 172966-31-3DP, oligonucleotide deriv. 172966-32-4DP, oligonucleotide deriv. 172966-33-5DP, oligonucleotide deriv. 172966-34-6DP, oligonucleotide deriv.
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(deprotection of; prepn. of arylacetyl-protected nucleotide derivs. for prepn. of oligonucleotides)

IT 92447-25-1P 132628-16-1P 172965-87-6P 172965-92-3P 172965-93-4P 172965-94-5P 172965-95-6P 172965-96-7P 172965-97-8P 172966-04-0P 172966-05-1P 172966-06-2P 172966-07-3P 172966-08-4P 172966-23-3P 172966-24-4P 172966-25-5P 172966-26-6P 172966-27-7P 172966-28-8P 172966-29-9P, N2-(3,4-Dichlorophenylacetyl)-2'-deoxyguanosine 172966-30-2P, N2-(4-Methoxyphenylacetyl)-2'-deoxyguanosine
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of arylacetyl-protected nucleotide derivs. for prepn. of oligonucleotides)

IT 130150-80-0P 172965-91-2P 172966-01-7P 172966-03-9P 172966-44-8P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of arylacetyl-protected nucleotide derivs. for prepn. of oligonucleotides)

IT 118-00-3DP, Guanosine, oligonucleotide derivs. 172965-88-7P 172965-89-8P 172965-90-1P 172965-98-9P 172965-99-0P 172966-00-6P 172966-09-5P 172966-10-8P 172966-11-9P 172966-12-0P 172966-13-1P 172966-14-2P 172966-15-3P 172966-17-5P 172966-19-7P 172966-20-0P 172966-21-1P 172966-22-2P 172966-35-7P 172966-36-8P 172966-37-9P 172966-38-0P 172966-39-1P 172966-40-4P 172966-41-5P 172966-42-6P 172966-43-7P

GI



AB 2',3'-Dideoxy-2',3'-didehydronucleosides [I; X = N, CH; Y = CR5; N; Z = CH, N; R4 = OH, NH2; R5 = H, (halo-substituted) CnH2nA or (CH2)mCH:CHA; m = 0-3; n = 1-3; A = H, F, Cl, Br, iodo], useful as antiviral agents, esp. against HIV, are prepd. in high yields and on a relatively large scale by subjecting various intermediates II-IV, V (R = Br, R1 = isobutyryloxy; or R = isobutyryloxy, R1 = Br) and VI to elimination reactions by treatment of (1) II with a strong base (e.g. tert-BuOK), (2) II with an org. acid in Ac2O at 120-160.degree. for 4-8 h followed by 5-O-deacetylation, (3) IV with P(OEt)3 in a polar solvent at 140-175.degree. 0.5-4 h, (4) V with Zn/Cu in an aprotic solvent, and (5) VI with a nonnucleophilic base (e.g. Bu4NF) or nucleophilic base (e.g. tert-BuOK and KOH). Thus, mesylation of thymidine with MeSO2Cl in pyridine at 0-5.degree. gave 81% 3',5'-di-O-(methanesulfonyl)thymidine which was added portionwise to a stirred soln. of aq. NaOH and then refluxed 2 h to give 74% 1-(3,5-anhydro-2-deoxy-.beta.-D-threo-pentofuranosyl)thymine. To a stirred soln. of 90.0 g of the latter octane was added 97% tert-BuOK (74 g) portionwise over 25 min at 18-22.degree. in an ice bath. The mixt. was stirred 1 h to give 57% 1-(2,3-dideoxy-.beta.-glycero-pent-2-enofuranosyl)thymine (VII). VII showed an IC50 of 0.33 .mu.M against HIV in CEM cells vs. 0.45 for AZT.

IC ICM C07D405-04
ICS A61K031-505

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1

ST dideoxydidehydronucleoside prepn HIV antiviral; pyrimidine nucleoside dideoxydidehydro prepn antiviral

IT Virucides and Virustats
(dideoxydidehydropyrimidine)
IT Immunodeficiency
(acquired immune deficiency syndrome, treatment of, dideoxydidehydropyrimidine nucleosides for)
IT Virus, animal
(human immunodeficiency, infection with, treatment of, dideoxydidehydropyrimidine nucleosides for)
IT Virus, animal
(human immunodeficiency 1, infection with, treatment of, dideoxydidehydropyrimidine nucleosides for)
IT Nucleosides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(pyrimidine, dideoxydidehydro, prepn. of, as antiviral agents against HIV)
IT 40635-67-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(bromination-acylation by, of uridine)
IT 58-96-8, Uridine
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with tri-Me orthoformate)
IT 149-73-5, Trimethyl orthoformate
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with uridine)
IT 122-52-1, Triethylphosphite
RL: RCT (Reactant); RACT (Reactant or reagent)
(elimination by, of (tritylthiocarbonylribofuranosyl)uracil)
IT 50-89-5, Thymidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(mesylation of, by methanesulfonyl chloride)
IT 56822-33-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclization of)
IT 42867-74-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deacetylation of)
IT 42867-75-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and elimination of)
IT 10270-39-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and elimination of, by triethylphosphite)
IT 16628-81-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and elimination reaction of)
IT 7481-90-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and elimination/ring opening reaction of)
IT 3056-17-5P 5974-93-6P, 2',3'-Dideoxy-2',3'-didehydrouridine
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antiviral agent against HIV)
IT 6160-65-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(thiocarbonylation by, of trityluridine)

IT 6554-10-5, 5'-O-Trityluridine
RL: RCT (Reactant); RACT (Reactant or reagent)
(thiocarbonylation of, by thiocarbonyldiimidazole)

L17 ANSWER 42 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 112:56592 MARPAT
TITLE: Preparation and formulation of 2',3'-dideoxy-2',2'-difluoronucleosides and anticancer and antiviral agents
INVENTOR(S): Hertel, Larry Wayne; Grossman, Cora Sue; Kroin, Julian Stanley
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 329348	A2	19890823	EP 1989-301309	19890210
EP 329348	A3	19900912		
EP 329348	B1	19950712		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8901076	A	19901031	ZA 1989-1076	19890210
CA 1312599	A1	19930112	CA 1989-590693	19890210
ES 2075040	T3	19951001	ES 1989-301309	19890210
DK 8900663	A	19890817	DK 1989-663	19890213
AU 8929926	A1	19890817	AU 1989-29926	19890214
AU 607840	B2	19910314		
HU 49366	A2	19890928	HU 1989-650	19890214
HU 203363	B	19910729		
CN 1035117	A	19890830	CN 1989-100441	19890215
JP 01249797	A2	19891005	JP 1989-35955	19890215
JP 3142128	B2	20010307		
US 5644043	A	19970701	US 1993-173256	19931227
US 5574021	A	19961112	US 1995-458110	19950602
PRIORITY APPLN. INFO.:			US 1988-156116	19880216
			US 1989-295321	19890111
			US 1989-394382	19890815
			US 1992-964121	19921021
			US 1993-173256	19931227

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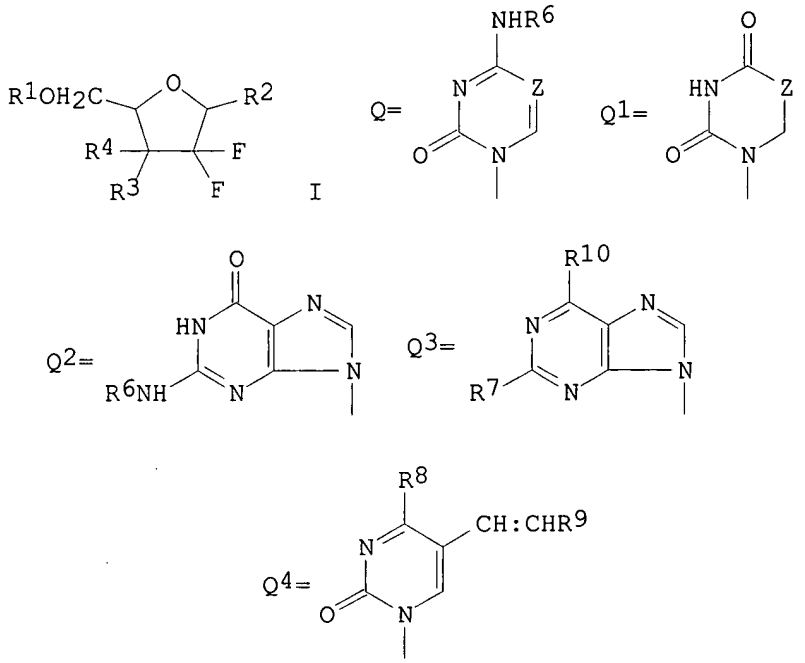

AB The title nucleosides [I; R1 = H, C1-4 alkyl, COR5; R2 = Q-Q4; R3 = H, NH2, N3, F; R4 = H, F; R5 = H, C1-4 alkyl; R6 = H, C1-4 alkyl, COR5; R7 = H, C1-4 (halo)alkyl, NH2, Br, F, Cl, iodo; R8 = OH, NH2; R9 = H, Br, Cl, iodo; R10 = NHR6, Br, Cl, OH, F, iodo; (presumably) Z = N, CR7], useful for treating susceptible neoplasms and viral infections in mammals, are prepd. Thus, acylation of .beta.-1-(4-amino-2-oxo-1H-pyrimidin-1-yl)-2-deoxy-2,2-difluororibose with pivaloyl chloride in 1H-(pyrimidin-1-yl)-5-O-pivaloyl-2-deoxy-2,2-difluororibose which was esterified with PhOC(S)Cl in pyridine contg. 4-dimethylaminopyridine, gave .beta.-1-(4-pivaloylamino-2-oxo-1H-pyrimidin-1-yl)-5-O-pivaloyl-3-O-phenoxythiocarbonyl-2-deoxy-2,2-difluororibose. Deoxygenation of the latter by treatment with Bu3Sn in the presence of 2,2'-azobis(2-methylpropionitrile) in PhMe at 85.degree. gave, after deacylation with concd. NH4OH in MeOH, .beta.-1-(4-amino-2-oxo-1H-pyrimidin-1-yl)-2,3-dideoxy-2,2-difluororibose (II). II in vitro inhibited human leukemia cells CCRF-CEM cell line with an IC50 value of 1.9 .mu.g/mL. Four I including II at 3.1-25 .mu.g/mL inhibited 27-50% herpes simplex virus 1. Two I at 25 and 13.5 .mu.g/mL inhibited 21 and 50%, resp. herpes simplex virus 2. II showed an IC50 value of 6.5 .mu.g/mL against Friends leukemia virus.

IC ICM C07H019-067
ICS C07H019-167; A61K031-70

ICA C07H005-02; C07H005-04

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 63

ST deoxyfluoronucleoside prepn anticancer antiviral; fluoronucleoside deoxy prepn anticancer antiviral; herpes simplex virus infection treatment deoxyfluoronucleoside

IT Nucleosides, compounds

RL: SPN (Synthetic preparation); PREP (Preparation)
(dideoxydifluoro, prepn. of, as anticancer and antiviral agents)
IT Neoplasm inhibitors
Virucides and Virustats
(dideoxydifluoronucleosides)
IT 3282-30-2, Pivaloyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation by, of (aminooxopyrimidinyl)deoxydifluororibose)
IT 1005-56-7, Phenyl chlorothionocarbonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation by, of (aminooxopyrimidinyl)deoxydifluororibose deriv.)
IT 95058-81-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation of, by pivaloyl chloride)
IT 124709-17-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation of, by triphenylmethyl chloride)
IT 95058-80-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of, by triphenylmethyl chloride)
IT 19597-69-4, Lithium azide
RL: RCT (Reactant); RACT (Reactant or reagent)
(azidolysis by, of pyrimidinyltrifluoromethyldeoxydifluororibose deriv.)
IT 124708-94-7P 124708-95-8P 124708-96-9P 124726-97-2P
124726-98-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as anticancer and antiviral agent)
IT 124708-97-0P 124708-98-1P 124708-99-2P 124709-00-8P
124709-01-9P 124709-02-0P 124709-03-1P 124709-04-2P
124709-05-3P 124709-06-4P 124709-07-5P 124709-08-6P
124709-09-7P 124709-10-0P 124709-11-1P 124709-12-2P
124709-13-3P 124709-14-4P 124709-15-5P 124709-16-6P
124726-99-4P 124816-42-8P 124816-43-9P 124816-44-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for anticancer and antiviral dideoxydifluoronucleoside)
IT 124709-18-8P 124709-19-9P 124709-20-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for anticancer and antiviral dideoxydifluororibose derivs.)
IT 18162-48-6, tert-Butyldimethylsilyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(silylation by, of dibenzoyldeoxydifluororibose)
IT 358-23-6, Triflic anhydride
RL: RCT (Reactant); RACT (Reactant or reagent)
(triflation by, of (methyldioxopyrimidinyl)deoxydifluororibose)
IT 76-83-5, Triphenylmethyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(tritylation by, of (methyldioxopyrimidinyl)deoxydifluororibose)

L17 ANSWER 43 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 111:97691 MARPAT
TITLE: Preparation of antiretroviral 2',3'-dideoxynucleoside dimers effective against human immunodeficiency virus (HIV)
INVENTOR(S): Broder, S.; Mitsuya, H.

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: U. S. Pat. Appl., 42 pp. Avail. NTIS Order No. PAT-5-646 31.
CODEN: XAXXAV
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 64631	A0	19880901	US 1987-64631	19870622
US 4837311	A	19890606		
DK 8803366	A	19881223	DK 1988-3366	19880620
EP 296573	A2	19881228	EP 1988-109952	19880622
EP 296573	A3	19900704		
EP 296573	B1	19940112		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL				
JP 02262587	A2	19901025	JP 1988-152457	19880622
AT 100098	E	19940115	AT 1988-109952	19880622
US 33887	E	19920414	US 1990-608431	19901102
PRIORITY APPLN. INFO.:			US 1987-64631	19870622
			EP 1988-109952	19880622

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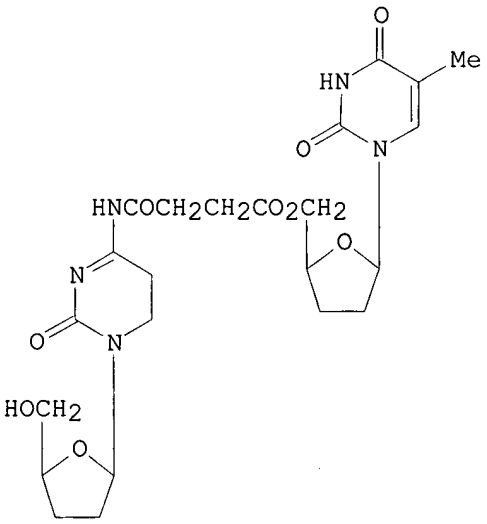

III

AB 2',3'-Dideoxynucleoside derivs. A-B-C [I; A, C = dideoxynucleoside radicals; B = linking group represented by C(:X)(CH2)nC(:X), C(:X),-C(:X)NHS(O)2, COCH2S(O)2, P(O)Me, P(O)O-, CO2(CH2)2S(O)2(CH2)2O2C, CO(CH2)2S2(CH2)2CO, CO(CH2)2O2C(CH2)2O2C(CH2)2CO; X = O, S; n = 2-6; and B is attached to A at either the 5'-OH position or the NH2 position of A; and C is attached to B at either the 5'-OH position or the NH2 position of C]

were prepd. as antiretroviral (particularly anti-HIV) agents. To a soln. of 0.57 mmol 3'-azido-3'-deoxythymidine 5'-(hydrogenbutanedioate) (II) (prepn. given) in pyridine were added 1.14 DCC and 1.14 mmol 1-hydroxybenzotriazole. After 2 h, 0.57 mmol 2',3'-dideoxy-5'-O-(tert-butyldimethylsilyl)cytidine was added and the mixt. was stirred 16 h at ambient temp. to give, after desilylation with Bu4NF in THF, nucleoside dimer III. III at 0.1-5 .mu.M in vitro showed equal or superior antiviral activity to 2',3'-dideoxycytidine or 3'-azido-3'-deoxythymidine alone against HIV.

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1

ST dideoxycytidine dimer prepn antiretroviral; azidodeoxythymidine contg dideoxycytidine prepn antiretroviral; dideoxyadenosine contg dideoxycytidine prepn antiretroviral; nucleoside dimer prepn antiretroviral; human immunodeficiency virus HIV antiviral

IT Virucides and Virustats
(against human immunodeficiency virus, nucleoside dimers contg. dideoxycytidine, azidodeoxythymidine or dideoxyadenosine)

IT Nucleosides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(dimers, contg. dideoxycytidine, azidodeoxythymidine, or dideoxyadenosine, prepn. of, as virucides against human immunodeficiency virus)

IT Virus, animal
(human immunodeficiency 1, infection by, treatment of, nucleoside dimers contg. dideoxycytidine, azidodeoxythymidine, or dideoxyadenosine for)

IT 108-55-4, Glutaric anhydride
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with dideoxycytidine deriv., in prepn. of virucide)

IT 4097-22-7, 2',3'-Dideoxyadenosine
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with N-(carboxybutyryl)dideoxy cytidine deriv., in prepn. of virucide)

IT 530-62-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with [(dimethylamino)methylene]cytidine)

IT 108-30-5, Succinic anhydride, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with azidodeoxythymidine, in prepn. of virucide)

IT 30516-87-1, 3'-Azido-3'-deoxythymidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with succinic anhydride, in prepn. of virucide)

IT 106060-83-7P 116504-10-0P 121892-92-0P 121892-93-1P
121892-94-2P 121892-95-3P 121892-96-4P 121892-97-5P
121892-98-6P 121892-99-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for dideoxycytidine-contg. nucleoside dimers)

IT 121892-89-5P 121892-90-8P 121892-91-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as virucide against human immunodeficiency virus)

IT 18162-48-6, tert-Butyldimethylsilyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)

(silylation by, of dideoxycytidine)
IT 7481-89-2, 2',3'-Dideoxycytidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(silylation of, by tert-butyldimethylsilyl chloride)
IT 4637-24-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(transacetalization of, with dideoxycytidine)

L17 ANSWER 44 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 109:222462 MARPAT
TITLE: Immunoglobulin conjugates with acylated difluoronucleosides having anticancer activity and their preparation
INVENTOR(S): Koppel, Gary Allen; Kennedy, George Davon; Armour, Henry Kenneth; Scott, William Leonard
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 272891	A2	19880629	EP 1987-311182	19871218
EP 272891	A3	19891108		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 4814438	A	19890321	US 1987-124191	19871123
SU 1787160	A3	19930107	SU 1987-4203967	19871216
DK 8706651	A	19880625	DK 1987-6651	19871217
AU 8782659	A1	19880630	AU 1987-82659	19871217
AU 590462	B2	19891102		
ZA 8709473	A	19890830	ZA 1987-9473	19871217
JP 63166897	A2	19880711	JP 1987-322619	19871218
CN 87108348	A	19880713	CN 1987-108348	19871218
CN 1018649	B	19921014		
HU 45547	A2	19880728	HU 1987-5862	19871218
HU 205135	B	19920330		
US 4994558	A	19910219	US 1989-294338	19890109
PRIORITY APPLN. INFO.:			US 1986-946351	19861224
			US 1987-124191	19871123

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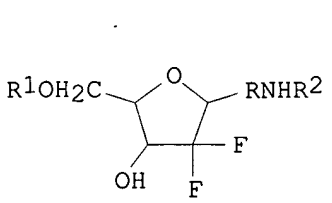

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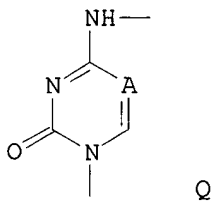

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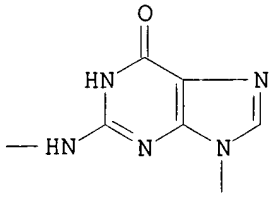

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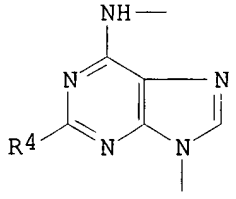


Q2

AB The anticancer acylated difluoronucleosides I (R1 = H, alkyl, COR3, COXCO; R2 = H, COXCO; R3 = H, alkyl; X = bond, alkylene, alkenylene, alkynylene, cycloalkylene, phenylene, hydroxyalkylene; RNH = Q, Q1, Q2; R4 = H, alkyl, NH2, halo; A = N, CR4; R1 .noteq. R2 = COXCO;) are conjugated to cancer cell-recognizing Igs. Succinic anhydride was added to a refluxing mixt. of 2'-deoxy-2,2'-difluorocytidine in dry EtOH to give 5'-O-(3-carboxy-1-oxopropyl)-2'-deoxy-2',2'-difluorocytidine, which was converted into the succinidoxy ester and conjugated with antibody 007B. The conjugate, injected 3 times at 5 mg/kg, inhibited the growth of exptl. P3-UCLA adenocarcinoma in rats.

IC ICM A61K039-395
ICS A61K047-00; A61K031-70

CC 1-6 (Pharmacology)
Section cross-reference(s): 15, 33

ST anticancer fluoronucleoside Ig conjugate; monoclonal antibody fluoronucleoside conjugate

IT Neoplasm inhibitors
(acylated difluoronucleosides, conjugated with Igs)

IT Neoplasm inhibitors
(adenocarcinoma, acylated difluoronucleosides, conjugated with Igs)

IT Immunoglobulins
RL: BIOL (Biological study)
(conjugates, with acylated difluoronucleoside anticancer agents)

IT Nucleosides, esters
RL: BIOL (Biological study)
(deoxyfluoro, esters, with dicarboxylic acids, reaction products with Igs, as target-directed neoplasm inhibitors)

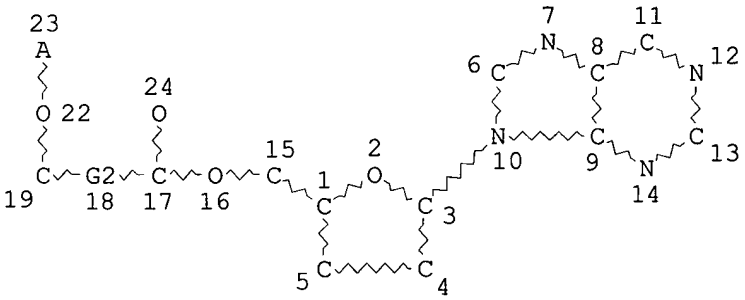
IT Antibodies
RL: BIOL (Biological study)
(monoclonal, conjugates with acylated difluoronucleoside antitumor agents)

IT 117702-06-4
RL: PRP (Properties)
(conjugation of, with monoclonal antibodies)

IT 117702-11-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for Ig-neoplasm inhibitor conjugates)

IT 117702-11-1DP, conjugate with Igs
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as target-directed neoplasm inhibitors)
IT 108-30-5, Succinic anhydride, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with deoxydifluorocytidine)
IT 95058-81-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with succinic anhydride)

FILE 'MARPATPREV' ENTERED AT 11:29:04 ON 03 APR 2003
L15 STR



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RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of arylacetyl-protected nucleotide derivs. for prepn. of oligonucleotides)

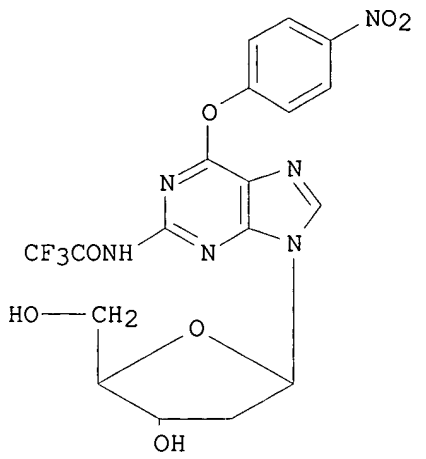
IT 92447-25-1DP, oligonucleotide deriv. 172966-23-3DP, oligonucleotide deriv. 172966-26-6DP, oligonucleotide deriv. 172966-27-7DP, oligonucleotide deriv.
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(stability of; prepn. of arylacetyl-protected nucleotide derivs. for prepn. of oligonucleotides)

IT 103-80-0, Phenylacetyl chloride 108-30-5, reactions 118-00-3, Guanosine, reactions 459-04-1, 4-Fluorophenylacetyl chloride 961-07-9, 2'-Deoxyguanosine 6834-42-0, 3-Methoxyphenylacetyl chloride 18162-48-6, tert-Butyldimethylsilyl chloride 37859-24-8, 4-Bromophenylacetyl chloride 40615-36-9, 4,4'-Dimethoxytrityl chloride 51747-24-1 89992-70-1 102691-36-1, 2-Cyanoethyl N,N,N',N'-tetraisopropylphosphorodiamidite
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; prepn. of arylacetyl-protected nucleotide derivs. for prepn. of oligonucleotides)

L17 ANSWER 26 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 123:83952 MARPAT
TITLE: 6-O-Substituted guanosine derivatives prepared by acylation and substitution reactions
INVENTOR(S): Jones, Roger A.; Fathip, Reza; Gaffney, Barbara L.
PATENT ASSIGNEE(S): Rutgers, The State University, USA
SOURCE: U.S., 24 pp. Cont. of U.S. Ser. No. 439,616, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5412088	A	19950502	US 1992-863653	19920403
PRIORITY APPLN. INFO.:			US 1989-439616	19891120

GI



I

AB The following species of N6-activated guanosine derivs. are disclosed: 2-N-trifluoroacetamido-6-(4-nitrophenoxy)-9-(2-deoxy-.beta.-D-erythro-pentofuranosyl)purine (I), 2-N-trifluoroacetamido-6-pentafluorophenoxy-9-(2-deoxy-.beta.-D-erythro-pentofuranosyl)purine, and 2-amino-6-(4-dimethylaminopyridinium)-9-(2-deoxy-.beta.-D-erythro-pentofuranosyl)purine. These guanosine compds. are useful as precursors in the synthesis of a wide variety of antiviral and anticancer nucleosides such as 2-amino-2-deoxyadenosine or 6-thio-deoxyguanosine. Also disclosed are oligonucleotides contg. the above nucleosides which are precursors to modified oligonucleotides which are useful as hybridization probes. Thus, e.g., 4 mmol deoxyguanosine was treated with 3.4 mL (24 mmol) of trifluoroacetic anhydride followed by 11.1 g (80 mmol) of 4-nitrophenol; workup afforded I in 67% yield.

IC ICM C07H019-167
ICS C07H019-173; C07H019-20; C07H021-04

NCL 536027810

CC 33-9 (Carbohydrates)

ST guanosine deriv acylation substitution

IT Substitution reaction
(6-O-substituted guanosine derivs. prepd. by acylation and substitution reactions)

IT Acylation
(trifloroacetylation; 6-O-substituted guanosine derivs. prepd. by acylation and substitution reactions)

IT 100-02-7, 4-Nitrophenol, reactions 108-18-9, Diisopropylamine 108-98-5, Thiophenol, reactions 109-78-4, 3-Hydroxypropionitrile 771-61-9, Pentafluorophenol 961-07-9, Deoxyguanosine 1122-58-3 51549-35-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(6-O-substituted guanosine derivs. prepd. by acylation and substitution reactions)

IT 76101-30-9P 102691-36-1P, 2-Cyanoethyl N,N,N',N'-tetraisopropylphosphorodiamidite 128790-76-1P 165290-72-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(6-O-substituted guanosine derivs. prepd. by acylation and substitution reactions)

IT 789-61-7P 964-21-6P 4546-70-7P 83024-94-6P 128790-73-8P
128790-74-9P 128790-75-0P 165290-73-3P 165290-74-4P
165290-75-5P 165337-46-2P 165337-47-3P 165337-48-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(6-O-substituted guanosine derivs. prepd. by acylation and substitution reactions)

L17 ANSWER 27 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 121:231270 MARPAT
TITLE: Preparation of siloxy-linked oligonucleotide analogs
INVENTOR(S): Walder, Joseph A.; Li, Zigun
PATENT ASSIGNEE(S): Integrated DNA Technologies, Inc., USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9406811	A1	19940331	WO 1993-US8980	19930922
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9351629	A1	19940412	AU 1993-51629	19930922
PRIORITY APPLN. INFO.:			US 1992-950384	19920923
			WO 1993-US8980	19930922

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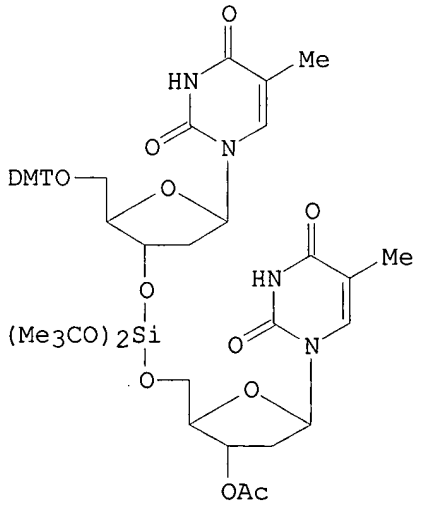


I

AB R1O(R3)(R2O)SiOY(Z)B (Z = protecting group; Y = pentose sugar; B = nucleic acid base; R1, R2 = apolar moieties; R3 = leaving group), and oligonucleotides thereof, were prepd. The siloxy-modified

oligonucleotides are easy to synthesize and exhibit nucleic acid hybridization properties essentially identical to those of unmodified oligonucleotides; the siloxy linkages are neutral, achiral, and are completely nuclease resistant. Thus, 5'-O-dimethoxytrityl-2'-deoxythymidine was dried by coevaporation with pyridine and dissolved in CH2Cl2/pyridine; this soln. was treated with (Me3CO)2SiCl2 (prepn. given) and the mixt. was stirred 3 h; 3'-acetyl-2'-deoxythymidine was added and the mixt. was stirred overnight to give 47% 5'-3' dimer I. This was deacetylated with NH4OH/EtOH (83%), a phosphoramidite group was added to the 3'-position (58%), and the siloxy dimer phosphoramidite was used in automated synthesis of 5' T-T-C-A-G-G-C-T-C-TSiT-C-T-C-A-G-C-G-T-T-C 3' (Si = di-tert-butoxysiloxy linkage; hyphen = phosphodiester linkage). The siloxy linkage had little effect on the stability of a duplex of this 21-mer with either a complimentary DNA or RNA oligonucleotide.

IC ICM C07H019-00
ICS C07H021-00; C07H017-00

CC 33-9 (Carbohydrates)
Section cross-reference(s): 29

ST siloxy oligonucleotide prepn

IT Nucleotides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(oligo-, prepn. of siloxy-linked)

IT 158135-14-9P
RL: SPN (Synthetic preparation); FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, in prepn. of siloxy oligonucleotides)

IT 158345-61-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 18395-80-7P, Di-tert-butoxydichlorosilane 158135-06-9P 158135-07-0P 158135-08-1P 158135-09-2P 158135-10-5P 158135-11-6P 158135-12-7P 158135-13-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for siloxy oligonucleotides)

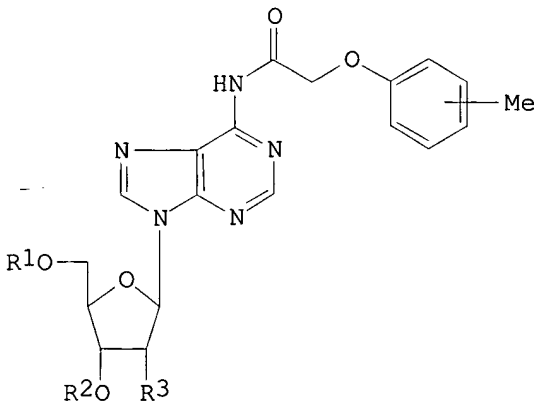
IT 75-65-0, tert-Butanol, reactions 124-40-3, Dimethylamine, reactions 10026-04-7, Silicon tetrachloride 21090-30-2 40615-39-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of siloxy oligonucleotides)

L17 ANSWER 28 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 121:158110 MARPAT
TITLE: Preparation of N6-(tolyloxyacetyl)adenosine or -2-deoxyadenosine derivative
INVENTOR(S): Horie, Yoji; Yoshida, Masao
PATENT ASSIGNEE(S): Toa Gosei Chem Ind, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06135989	A2	19940517	JP 1992-308093	19921022

PRIORITY APPLN. INFO.: JP 1992-308093 19921022

GI



I

AB The title compds. (I; R1 = H, trityl, alkoxytrityl, tolyloxyacetyl; R2 = H; R3 = H, OH), useful as intermediates for oligonucleotides, are prepd. The tolyloxyacetyl protective group of I show appropriate stability against the base treatment during the oligonucleotide synthesis, possibly due to the electron-donating Me group which moderately strengthens the amide bond, is readily deprotected under mild conditions using an alkali without the formation of side products, and thus facilitates the synthesis and purifn. of oligonucleotides. Phosphorylation of I with a phosphorylating agent at 3'-OH group gives a mononucleotide unit for the oligonucleotide synthesis and esterification with succinic anhydride introduces a carboxy group which in turn is condensed with a functionalized solid support to provide a nucleotide solid support. Thus, 0.50 g 2'-deoxyadenosine was coevaporated twice with pyridine, suspended in anhyd. pyridine with stirring followed by adding 10 mmol Me3SiCl and after stirring for 30 min, 2.7 mmol p-tolyloxyacetyl chloride was added followed by stirring for 90 min to give an intermediate I (Me is disposed at 4-position; R1 = R2 = R3 = H) and pyridine hydrochloride. The latter mixt. was coevaporated twice with pyridine and suspended in anhyd. pyridine followed by adding 2 mmol 4,4'-dimethoxytrityl chloride and stirring the resulting mixt. for 2 h to give, after silica gel chromatog., 55% I (Me is disposed at 4-position; R1 = 4,4'-dimethoxytrityl, R2 = R3 = H).

IC ICM C07H019-167
ICS C07H019-173
CC 33-9 (Carbohydrates)
ST tolyloxyacetyldeoxyadenosine deriv prepn intermediate oligonucleotide; tolyloxyacetyl amino protective group deoxyadenosine
IT Protective groups
(tolyloxyacetyl, for amino group of adenosine and deoxyadenosine in oligonucleotide synthesis)
IT Nucleotides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(oligo-, intermediate for prepn. of, N-(tolyloxyacetyl)adenosine

and -deoxyadenosine derivs. as)
IT 15516-47-9, p-Tolyloxyacetyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation by, of trimethylsilylated deoxyadenosine)
IT 157402-06-7P, N6-(p-Tolyloxyacetyl)-2'-deoxyadenosine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and tritylation of, by dimethoxytrityl chloride)
IT 157402-05-6P, 5'-O-(4,4'-Dimethoxytrityl)-N6-(p-tolyloxyacetyl)-2'-deoxyadenosine
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for oligonucleotide synthesis)
IT 958-09-8, 2'-Deoxyadenosine
RL: RCT (Reactant); RACT (Reactant or reagent)
(silylation with trimethylsilyl chloride and acylation of, by p-tolyloxyacetyl chloride)
IT 40615-36-9, 4,4'-Dimethoxytrityl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(tritylation by, of N-(tolyloxyacetyl)deoxyadenosine)

L17 ANSWER 29 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 121:9934 MARPAT
TITLE: Pentavalent synthesis of oligonucleotides containing stereospecific alkylphosphonates and arylphosphonates
INVENTOR(S): Wickstrom, Eric; Lebedev, Alexander V.
PATENT ASSIGNEE(S): Research Corp. Technologies, Inc., USA
SOURCE: PCT Int. Appl., 233 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9400473	A2	19940106	WO 1993-US6277	19930630
WO 9400473	A3	19940217		
W: AU, CA, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9346611	A1	19940124	AU 1993-46611	19930630
PRIORITY APPLN. INFO.:			US 1992-907771	19920630
			WO 1993-US6277	19930630

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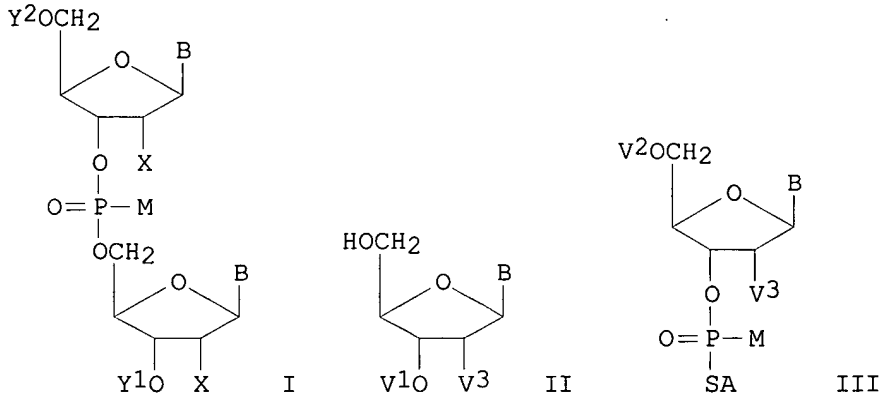


AB The present invention provides a method for making R stereospecific alkyl- and aryl-phosphonate linkages between nucleotides. These methods can be used for automated synthesis of oligonucleotides having sequential R stereospecific alkyl- and aryl-phosphonate linkages. The present invention is also directed to the oligonucleotides having several sequential R phosphonate linkages which were produced by the subject methods. Moreover, the present invention provides methods for using the subject oligonucleotides, including methods for regulating the biosynthesis of a DNA, and RNA or a protein and methods for detecting and isolating complementary nucleic acid targets. Title oligonucleotides [I; Y1 = H, phosphate, V1; Y2 = H, phosphate, V2; X = OH, V3; M = alkyl, cycloalkyl, thioxo, etc.; B = (un)substituted purine or pyrimidine residue; V1 = protecting group, solid support, or phosphate attached to the penultimate nucleotide of said oligonucleotide; V2 = protecting group; V3 = H, O-Y3; Y3 = alkyl protecting group; A = activating group] and their intermediates are prepd. E.g., 5'-(dimethoxytrityl)thymidyl 3'-methylphosphonoamidate was protected by cyanoethylation in the presence of 4-(N,N-diethylamino)pyridine and (CF3CO)2O at room temp. to give 5'-(dimethoxytrityl)thymidyl 3'-[2-cyanoethyl methylphosphonate], whose oxidn. with sulfur (S8) in the presence of MeCN gave the diastereomers of 5'-(dimethoxytrityl)thymidyl 3'-[2-cyanoethyl methylphosphonothioate], which were sepd. and purified by HPLC; cyanoethyl groups were removed with concd. NH4OH in EtOH, the deprotected diastereomers were then purified by silica HPLC and the ammonium cation was replaced with Li+ by using a Dowex 50W .times. 2 exchange column to yield the lithium salts of sep. Sp- and Rp-stereoisomers of 5'-(dimethoxytrityl)thymidyl 3'-methylphosphonothioate. Sp- and Rp-stereoisomers prepd. as above were stable and were sepd. by ion exchange chromatog. or by HPLC using anhyd. or aq. solvents. The Sp-stereoisomer is reacted with an activator, e.g., 2-chloro-N-methylpyridinium, the intermediate (with retention of configuration) then undergoes an SN2 replacement reaction with a 5'-unprotected nucleoside to give the Rp-configurated dinucleotide; the displaced 2-thio-N-methylpyridinium mol. is stabilized by resonance tautomerization and does not react with the phosphorus to cause epimerization of the R configuration. A compartmentalized kit for producing a polynucleotide chain of an oligonucleotide having at least 5

sequential R-alkylphosphonate or R-arylphosphonate linkages are claimed. These methods may be used in correcting genetic disorders, e.g., Alzheimer's disease, by inhibiting the prodn. of mutants or over-produced proteins.

IC ICM C07H021-00
ICS C12Q001-68; A61K031-70

CC 33-10 (Carbohydrates)
Section cross-reference(s): 1, 3

ST R configurated phosphonate linkage oligonucleotide; genetic disorder phosphonate linkage oligonucleotide

IT Nucleic acids
RL: SPN (Synthetic preparation); PREP (Preparation)
(contg. stereoselective phosphonate linkages, prepn. of)

IT Mental disorder
(Alzheimer's disease, inhibiting prodn. of mutants or over-produced proteins involved in, methods for)

IT 129395-80-8P 129395-83-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for synthesis of nucleic acids with stereoselective phosphonate linkages)

L17 ANSWER 30 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 120:324141 MARPAT
TITLE: Trivalent synthesis of oligonucleotides containing stereospecific alkylphosphonates and arylphosphonates
INVENTOR(S): Wickstrom, Eric; Rife, Jason P.
PATENT ASSIGNEE(S): Research Corp. Technologies, Inc., USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9400472	A2	19940106	WO 1993-US6251	19930630
WO 9400472	A3	19940217		
W: AU, CA, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9346598	A1	19940124	AU 1993-46598	19930630

PRIORITY APPLN. INFO.: US 1992-907768 19920630
WO 1993-US6251 19930630

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Oligonucleotides contg. (R)-alkylphosphonate and -arylphosphonate linkages [I; Y1 = H, phosphate, phosphate present in said nucleotide, protecting group, solid support, phosphate present on the penultimate nucleotide of said oligonucleotide; Y2 = H, phosphate, phosphate present in said oligonucleotide, protecting group; X = H, (un)protected OH, alkoxy; B = (un)substituted purine

or pyrimidine base; M = alkyl, cycloalkyl, thioxo, alkylthio, (un)substituted aryl or arylalkyl] are prepd. by reacting a 5'-O-activated nucleotide [II; A = activating group; B = same as above; V1 = protecting group, solid support, phosphate present on the penultimate nucleotide of said oligonucleotide; V3 = H, (un)protected OH, alkoxy] with an alkyl- or arylphosphinate nucleotide intermediate (III; V2 = protecting group; B, M, V3 = same as above) under conditions to produce a S stereoisomeric alkyl- or arylphosphonate linkage of dinucleotide (IV). This process provides a method for making R stereospecific alkyl- and aryl-phosphonate linkages between nucleotides. These methods can be used for automated synthesis of oligonucleotides having sequential R stereospecific alkyl- and aryl-phosphonate linkages. The present invention is also directed to the oligonucleotides having several sequential R phosphonate linkages which were produced by the subject methods. Moreover, the present invention provides methods for using the subject oligonucleotides, including methods for regulating the biosynthesis of DNA, RNA or a protein and methods for detecting and isolating complementary nucleic acid targets. These oligonucleotides show increased nuclease resistance and cell penetration, and particularly improved binding properties to DNA and RNA compared to S stereoisomers, and are useful as diagnostic probes and therapeutic agents (no data). Thus, 5'-iodo-3'-O-acetyl-dideoxynucleoside (V) was reacted with CF3SO3Ag to give 5'-O-activated nucleoside triflate II (A = CF3SO2, V1 = Ac, V3 = H) (IIA). 3'-O-methylphosphonoamidite nucleotide (VI) was hydrolyzed in the presence of tetrazole in H2O to give a racemic methylphosphinate (RS)-III (V2 = DMT, V3 = H) which are stable and can be sepd. by AcOH/MeOH-washed silica with CHCl3/MeOH elution to give (S)-III (V2 = DMT, V3 = H). The latter S-enantiomer was coupled with nucleoside triflate IIA at the 5'-position without altering the S phosphorus configuration to give (S)-methylphosphonate dinucleotide IV (V1 = Ac, V2 = DMT, V3 = H, M = Me). The stereoisomeric configuration of a phosphonate linkage was detected and monitored by CD and 1H and 31P NMR.

IC ICM C07H021-00
ICS C12Q001-68; A61K031-70

CC 33-9 (Carbohydrates)
Section cross-reference(s): 9

ST oligonucleotide stereospecific alkylphosphonate prepn; arylphosphonate oligonucleotide prepn diagnostic therapeutic agent

IT Nucleic acid hybridization
(probes for, (R)-alkylphosphonate- and (R)-arylphosphonate-contg. oligonucleotides as)

IT Diagnosis
(agents, (R)-alkylphosphonate- and (R)-arylphosphonate-contg. oligonucleotides as)

IT Nucleotides, polymers
RL: SPN (Synthetic preparation); PREP (Preparation)
(oligo-, (R)-alkylphosphonate- and (R)-arylphosphonate-contg., prepn. of, by coupling of nucleoside 3'-aryl- or alkylphsophinate with 5'-O-activated nucleosides, as diagnostic and therapeutic agents)

IT Nucleotides, polymers
RL: SPN (Synthetic preparation); PREP (Preparation)
(oligo-, antisense, (R)-alkylphosphonate- and (R)-arylphosphonate-contg., prepn. of, as therapeutic agents)

IT 155097-60-2P 155158-42-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and sepn. of, from (R)-stereoisomer)

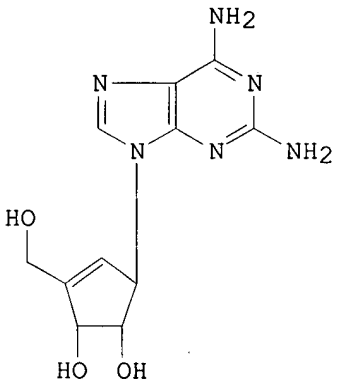
IT 155097-58-8P 155097-61-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for methylphosphonate-contg. oligonucleotides)

IT 155097-59-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, method for)

L17 ANSWER 31 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 119:271643 MARPAT
TITLE: Preparation of 2-aminoneplanocin A as antiviral agents
INVENTOR(S): Ohara, Takumi; Shuto, Satoshi; Kosugi, Yoshinori; Yaso, Masao; Yokoiyama, Shigeyuki
PATENT ASSIGNEE(S): Asahi Chemical Ind, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05170765	A2	19930709	JP 1991-357285	19911225

PRIORITY APPLN. INFO.: JP 1991-357285 19911225
OTHER SOURCE(S): CASREACT 119:271643
GI



I

AB The title compd. I, useful as an antiviral agent, was prepd. as follows. Treatment of 2.6-diaminopurine with NaH in DMF, followed by reaction with (1S, 2S, 3R)-1-p-toluenesulfonyloxy-4-(benzyloxymethyl)-2,3-isopropylidenedioxy-4-cyclopentene and deprotection, gave I. I in vitro showed MIC of 3.9 .mu.g/ML against bovine stomatitis virus.

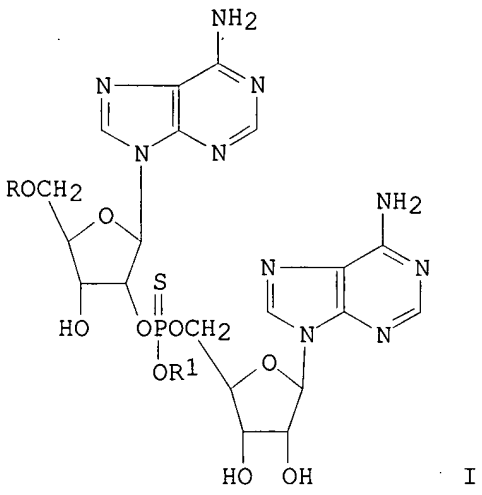
IC ICM C07D473-16

ICS A61K031-52
CC 33-9 (Carbohydrates)
Section cross-reference(s): 1
ST aminoneplanocin A prepn virucide
IT Virucides and Virustats
(aminoeplanocin A)
IT 151519-55-0P, 2-Aminoneplanocin A
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as antiviral agent)
IT 151293-88-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, in prepn. of antiviral agent)
IT 100806-47-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with purine deriv.)
IT 1904-98-9, 2,6-Diaminopurine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with toluenesulfonyloxycyclopentene deriv.)

L17 ANSWER 32 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 119:9107 MARPAT
TITLE: 2',5'-nucleotide analogs as antiviral agents
INVENTOR(S): Battistini, Carlo; Brasca, Maria Gabriella; Giordani, Antonio; Fustinoni, Silvia; Ermoli, Antonella
PATENT ASSIGNEE(S): Farmitalia Carlo Erba S.r.l., Italy
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9221691	A1	19921210	WO 1992-EP1058	19920514
W: JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
EP 541742	A1	19930519	EP 1992-909806	19920514
R: DE, GB, IT				
JP 06500568	T2	19940120	JP 1992-509190	19920514
PRIORITY APPLN. INFO.:			GB 1991-11967	19910604
			WO 1992-EP1058	19920514

GI



I

AB Thionucleotides I (R = H, 2'- or 3'-thionucleotidyl conjugated at its 5' position with an acyl group, phosphonyl, thiophosphonyl, (un)esterified alkylphosphonate, acyl; R1 = H, alkyl) were prepd. Thus, N6-benzoyl-3',5'-o-(1,1,3,3-tetraisopropyl-1,3-disiloxanediyl)adenosine was phosphonylated with PCl3-Et3N.H2CO3, coupled with N6-benzoyl-2',3'-o-(1,1,3,3-tetraisopropyl-1,3-disiolxanediyl)adenosine, and deblocked to give (Sp)-I (R = H, R1 = Na). At 400 .mu.m (Sp)-I (R = H, R1 = Na) caused 80% inhibition of Herpes simplex virus type 1 growth.

IC ICM C07H021-00
ICS A61K031-70

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1

ST adenine thiodinucleotide prepn virucide; thioadenylyladenosine prepn virucide

IT Virucides and Virustats
(thioadenylyladenosine derivs.)

IT 124-07-2, Octanoic acid, reactions 5292-21-7, Cyclohexylacetic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation by, of thioadenylyladenosine)

IT 57-88-5, Cholesterol, reactions 30334-71-5 79154-57-7 81256-88-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(phosphonylation of)

IT 142025-24-9P 142129-29-1P 147632-85-7P 147632-99-3P 147633-01-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and debenzoylation of)

IT 142025-22-7P 142129-33-7P 147632-68-6P 147632-90-4P 147632-93-7P 147633-06-5P 147633-09-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deblocking of)

IT 147632-65-3P 147632-71-1P 147632-74-4P 147632-76-6P 147632-79-9P 147632-82-4P 147632-87-9P 147632-96-0P

147633-03-2P 147633-11-2P 147730-71-0P 147730-74-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and desilylation of)

IT 142025-18-1P 142025-28-3P 142129-31-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and detritylation of)

IT 142025-30-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with adenosine phosphonate)

IT 147633-07-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with lysine deriv.)

IT 142025-14-7P 142025-16-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with protected adenosine)

IT 1510-21-0P 137714-54-6P 147632-69-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with thioadenylyladenosine)

IT 90108-21-7P 147632-63-1P 147632-77-7P 147632-88-0P
147730-76-5P 147730-77-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and virucidal activity of)

IT 142025-20-5P 142025-26-1P 147632-66-4P 147632-72-2P
147632-75-5P 147632-80-2P 147632-83-5P 147632-91-5P
147632-94-8P 147632-97-1P 147633-04-3P 147633-10-1P
147660-36-4P 147730-69-6P 147730-75-4P 147732-09-0P
148035-10-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 79974-68-8 135732-99-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with adenosine phosphonate)

IT 147632-67-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with cholesteryl phosphonate)

IT 147730-72-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with lysine deriv.)

IT 57-10-3, Palmitic acid, reactions 2389-60-8 3303-84-2
6404-29-1 13734-34-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with thioadenylyladenosine)

L17 ANSWER 33 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 117:151294 MARPAT
TITLE: Preparation of 2-substitute cycloalkylalkynyladenosine derivatives as antihypertensives with high selectivity for A2 receptors
INVENTOR(S): Miyashita, Takanori; Abiru, Toichi; Watanabe,

Yoko; Yamaguchi, Toyofumi; Matsuda, Akira
PATENT ASSIGNEE(S): Yamasa Shoyu K. K., Japan
SOURCE: Eur. Pat. Appl., 37 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 488336	A1	19920603	EP 1991-120461	19911129
EP 488336	B1	19950510		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 05163294	A2	19930629	JP 1991-34249	19910228
JP 3025541	B2	20000327		
US 5189027	A	19930223	US 1991-799071	19911127
CA 2056596	AA	19920531	CA 1991-2056596	19911128
CA 2056596	C	20010821		
AT 122355	E	19950515	AT 1991-120461	19911129
ES 2073653	T3	19950816	ES 1991-120461	19911129
PRIORITY APPLN. INFO.:			JP 1990-337273	19901130
			JP 1991-34249	19910228

GI For diagram(s), see printed CA Issue.

AB Title compds. I (R = H, OH; R1,R2,R3 = H, PO3H2, hydroxyl protective group, m = 2-7; n = 0-3, were prepd. for use as antihypertensives. Thus, 2-iodoadenosine was coupled with 3-cyclopentylpropyne in presence of Pd(PPh3)2Cl2-CuI to give 70% I (R = H, R1-R3 = H, m = 4, n = 1, II). II had an affinity const. for A2 receptors of 2.3 nM and an antihypertensive ED30 of 0.054 .mu.g/kg i.v. in rats.

IC ICM C07H019-167
ICS A61K031-70
CC 33-9 (Carbohydrates)
Section cross-reference(s): 1
ST nucleoside cycloalkylalkynyl prepn adenosine receptor; antihypertensive adenosine cycloalkylalkynyl

IT Antihypertensives
(cycloalkylalkynyl adenosine derivs. as)

IT Receptors
RL: PROC (Process)
(purinergic A2, binding of, with cycloalkylalkynyl adenosine derivs.)

IT 141018-25-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(benzylation of)

IT 35109-88-7, 2-Iodoadenosine
RL: RCT (Reactant); RACT (Reactant or reagent)
(coupling of, with cycloalkyne)

IT 5987-76-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(coupling of, with ethenylcyclopentanol)

IT 78-27-3, 1-Ethynyl-1-cyclohexanol 931-48-6, Cyclohexylacetylene 116279-08-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(coupling of, with iodoadenosine)

IT 17356-19-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(coupling of, with nucleoside)

IT 930-51-8 2809-78-1 5963-75-7 17715-00-3 55373-76-7
141345-07-5 141345-08-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(coupling of, with nucleosides)
IT 141345-31-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and aminolysis of)
IT 143483-94-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and coupling of, with ethenylcyclohexanol)
IT 141345-24-6P 141345-26-8P 141345-28-0P 141345-29-1P
141345-30-4P 141345-33-7P 141345-34-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deblocking of)
IT 143483-95-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and deisopropylidenation of)
IT 141345-09-7P 141345-11-1P 141345-12-2P 141345-14-4P
141345-15-5P 141345-17-7P 141345-19-9P 143483-93-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT 141345-10-0P 141345-13-3P 141345-18-8P 141345-20-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., antihypertensive, and affinity const. for adenosine receptors of)

L17 ANSWER 34 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 117:111992 MARPAT
TITLE: Phosphonate derivatives of certain nucleosides
INVENTOR(S): Halazy, Serge; Casara, Patrick; Neises, Bernhard; Jund, Karin
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals, Inc., USA
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 477454	A1	19920401	EP 1990-402695	19900928
R: FR				
EP 479640	A2	19920408	EP 1991-402517	19910923
EP 479640	A3	19930127		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 04316589	A2	19921106	JP 1991-274878	19910927

PRIORITY APPLN. INFO.: EP 1990-402695 19900928
GI For diagram(s), see printed CA Issue.
AB Title phosphonates I [B = (un)substituted purinyl, pyrimidinyl, triazinyl, triazolyl, thiazolyl, selenazolyl; R = (un)substituted alkyl; R1 = N3, F, Cl, OH, H; R2 = H, Cl, F, OH; R3 = H, Et; X = alkylene, oxaalkylene which may be unsatd. and/or substituted] and their 2',3'-didehydro analogs were prepd. for use as virucides, bactericides, and neoplasm inhibitors (no data). Thus,

3'-fluoro-2',3'-dideoxy-5-chlorouridine was treated with 2-bromoacetonyltetrahydropyran followed by CF3P(O)(OH)2 to give the phosphinate II.

IC ICM C07H019-10
ICS C07H019-20; A61K031-70

CC 33-9 (Carbohydrates)

ST nucleoside phosphinate phosphonate; virucide nucleoside phosphinate phosphonate; bactericide nucleoside phosphinate phosphonate; neoplasm inhibitor nucleoside phosphinate phosphonate

IT Bactericides, Disinfectants, and Antiseptics
Neoplasm inhibitors
Virucides and Virustats
(nucleoside phosphinate and phosphonate derivs.)

IT Nucleosides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(phosphinate and phosphonate derivs., prepn. of)

IT 142685-06-1P 142706-35-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and desilylation of)

IT 142684-92-2P 142685-01-6P 142685-04-9P 142685-08-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and ester hydrolysis of)

IT 143054-81-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and oxidn. of)

IT 142684-98-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with azidodeoxythymidine)

IT 142684-88-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with butylphosphonic acid)

IT 126181-58-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with dideoxyguanosine)

IT 142684-94-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with dideoxyinosine)

IT 142685-07-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with difluorobutynylphosphonate)

IT 142685-00-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with difluoromethyl phosphate)

IT 142684-90-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with methanephosphonic acid)

IT 142684-86-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

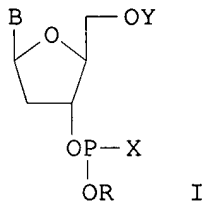
RACT (Reactant or reagent)
(prepn. and reaction of, with trifluoromethanephosphonic acid)
IT 142684-96-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(prepn. and redn. of)
IT 142684-87-5P 142684-89-7P 142684-91-1P 142684-93-3P
142684-95-5P 142684-97-7P 142684-99-9P 142685-02-7P
142685-05-0P 142685-09-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT 52103-12-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with azidodeoxythymidine)
IT 119644-22-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with bromo(tetrahydropyranyloxy)acetone)
IT 69655-05-6, 2',3'-Dideoxyinosine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with bromobutylphosphonate)
IT 1478-53-1, Diethyl difluoromethylphosphonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with dibromopropane ot thymidine deriv.)
IT 31618-90-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with dideoxydidehydrothymidine)
IT 38002-45-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with difluoromethanephosphonate)
IT 109-64-8, 1,3-Dibromopropane
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with difluoromethylphosphonate)
IT 40274-28-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with dihydrodideoxythymidine)
IT 116731-32-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with fluorodideoxyuridine)
IT 993-13-5, Methanephosphonic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with hydroxypropylthymidine deriv.)
IT 3416-05-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tetrahydropyranyloxybutynyl bromide)
IT 30516-87-1, 3'-Azido-3'-deoxythymidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tetrahydropyranyloxypropyl iodide, or
triflation of)
IT 3321-64-0, Butylphosphonic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with thymidine deriv.)
IT 3056-17-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tosyloxymethylphosphonate)
IT 374-09-4, Trifluoromethanephosphonic acid 142684-85-3
142685-03-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with uridine deriv.)

IT 109-86-4 85326-06-3, 2',3'-Dideoxyguanosine
RL: RCT (Reactant); RACT (Reactant or reagent)
(triflation of)

L17 ANSWER 35 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 117:27055 MARPAT
TITLE: Preparation of antisense L- and DL-oligodeoxyribonucleotides
INVENTOR(S): Shudo, Koichi; Hashimoto, Yuichi; Fujimori, Shizuyoshi
PATENT ASSIGNEE(S): Japan
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9201704	A1	19920206	WO 1991-JP1007	19910726
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2083445	AA	19920127	CA 1991-2083485	19910726
AU 9182246	A1	19920218	AU 1991-82246	19910726
EP 540742	A1	19930512	EP 1991-913310	19910726
R: CH, DE, ES, FR, GB, IT, LI, NL				
JP 3119871	B2	20001225	JP 1991-512383	19910726
PRIORITY APPLN. INFO.:			JP 1990-198123	19900726
			WO 1991-JP1007	19910726

GI



I

AB The title oligodeoxynucleotides, having 2-deoxy-.beta.-L-erythro-pentofuranose-contg. L-nucleosides and/or alternately natural D-nucleosides linked with each other through 3' .fwdarw. 5' phosphodiester linkages, are prepd. by the solid phase method using L-nucleoside phosphoramidites [I; B = (un)protected nucleic acid base; R = cyanoethyl, alkyl; X = (un)protected amino; Y = OH-protecting group] (prepn. given). The oligodeoxynucleotide combines specifically with a natural oligonucleotide, RNA, or DNA having a complementary base sequence and is useful as an antisense DNA having an activity of inhibiting gene expression and as a virucide. Thus, (L-dA)6, (L-dX)12 (X = A, T, C, G), L-AATACTCATACTCTTC, and (DL-dA)12 were prepd. by the solid phase method. (DL-DA)12 was hardly hydrolyzed by bovine and snake venom

phosphoesterase in 40 min. PolyU-(DL-dA)12 and polyU-(L-dA)12 complexes showed melting temps. (Tm) of 6.5.degree. and (53.5 and 68.5.degree.), resp., vs. 72.5.degree. for polyU-(D-dA)12 complex.
IC ICM C07H021-04
CC 33-9 (Carbohydrates)
ST antisense oligodeoxyribonucleotide prepn virucide
IT Virucides and Virustats
(antisense L- and DL- oligodeoxyribonucleotides)
IT Nucleotides, polymers
RL: SPN (Synthetic preparation); PREP (Preparation)
(oligo-, deoxyribo-, antisense, L- and DL-, prepn. of, as virucides)
IT 129491-61-8P 141732-04-9P 141771-58-6P 141789-73-3P
141933-55-3P 141961-28-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antisense DNA and virucide)
IT 3056-13-1P 3424-98-4P 7288-28-0P 22837-44-1P 40093-94-5P
131607-27-7P 141771-59-7P 141771-60-0P 141771-61-1P
141771-62-2P 141771-63-3P 141771-64-4P 141771-66-6P
141771-67-7P 141771-68-8P 141771-69-9P 141771-71-3P
141771-72-4P 141771-73-5P 141771-74-6P 141771-75-7P
141771-76-8P 141771-77-9P 141771-78-0P 141771-79-1P
141771-80-4P 141789-74-4P 141846-54-0P 141846-55-1P
141846-56-2P 141846-57-3P 141847-24-7P 141847-62-3P
141933-61-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for antisense L- and DL-oligodeoxyribonucleotides)
IT 65-71-4 66-22-8, Uracil, reactions 97-72-3, Isobutyric anhydride
98-88-4, Benzoyl chloride 109-78-4 7220-39-5 10310-21-1,
2-Amino-6-chloropurine 14365-45-8 18546-37-7, 2-Deoxy-L-ribose
40615-36-9, 4,4'-Dimethoxytrityl chloride 89992-70-1 141846-58-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of antisense L- and DL-oligodeoxyribonucleotides)

L17 ANSWER 36 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 116:174680 MARPAT
TITLE: Preparation of ether lipid-nucleoside covalent conjugates as HIV-1 inhibitors.
INVENTOR(S): Piantadosi, Claude; Marasco, Canio J., Jr.; Kucera, Louis S.
PATENT ASSIGNEE(S): Wake Forest University, USA; University of North Carolina
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9119726	A1	19911226	WO 1991-US4289	19910614

W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, RO, SD, SE, SU, US
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG

CA 2085354	AA	19911216	CA 1991-2085354	19910614
AU 9180597	A1	19920107	AU 1991-80597	19910614
AU 660417	B2	19950629		
EP 533825	A1	19930331	EP 1991-912194	19910614
EP 533825	B1	19960424		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05507929	T2	19931111	JP 1991-511531	19910614
AT 137242	E	19960515	AT 1991-912194	19910614
PRIORITY APPLN. INFO.:			US 1990-539001	19900615
			WO 1991-US4289	19910614

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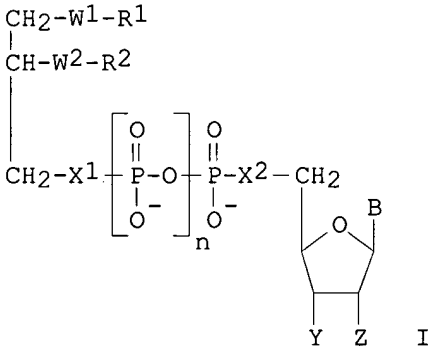

AB The title compds. [I; R1 = alkyl, alkenyl; R2 = H, alkyl, alkenyl; W1 = S, O, NHCO, NH; W2 = S, O, NHCO, OCO, NH, bond; n = 0, 1; X1, X2 = O, bond; with provisos; Y = H, F, N3; Z = H, F; or YZ = bond; B = nucleoside base, e.g., adenine, thymine, cytosine residue] were prepd. 3-Octadecanamido-2-ethoxypropyl diphenyl phosphate (prepn. given) was hydrogenolyzed to give 3-octadecanamido-2-ethoxypropyl dihydrogen phosphate, which was condensed with AZT to give I [B = thymine residue; W1 = NHCO, W2 = O, R1 = (CH2)16Me, R2 = Et, X1 = X2 = O, n = 0, Y = N3, Z = H]. In an in vitro study using HIV-1-infected CEM-SS cells and AZT and dideoxyinosine as controls, I had IC50 values ranging from 0.02-1.56 .mu.M.

IC ICM C07H017-00
ICS A61K031-70

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 34

ST lipid nucleoside prepn antiviral; HIV inhibitor lipid nucleoside

IT Virucides and Virustats
(lipid-nucleoside covalent conjugates)

IT Nucleosides, compounds
RL: SPN (Synthetic preparation); PREP (Preparation)
(conjugates, with lipids, prepn. of, as HIV-1 inhibitors)

IT Lipids, compounds
RL: SPN (Synthetic preparation); PREP (Preparation)
(conjugates, with nucleosides, prepn. of, as HIV-1 inhibitors)

IT Virus, animal
(human immunodeficiency 1, inhibitors, ether lipid-nucleoside covalent conjugates as)

IT 112988-98-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with di-Ph chlorophosphate)
IT 10025-87-3, Phosphorus oxychloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with dialkylglycerol)
IT 2524-64-3, Diphenyl chlorophosphate
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with glycerol deriv.)
IT 92758-87-7 131933-72-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with phosphorus oxychloride)
IT 30516-87-1, AZT
RL: RCT (Reactant); RACT (Reactant or reagent)
(phosphorylation of, with glycerol phosphate deriv.)
IT 139964-27-5P 139964-28-6P 139964-29-7P 139964-30-0P
139964-31-1P 139964-32-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as HIV-1 inhibitor)
IT 131933-59-0P 131933-65-8P 131933-66-9P 131933-69-2P
131933-72-7P 139964-33-3P 139964-34-4P 139964-35-5P
139964-37-7P 139964-38-8P 139964-40-2P 139964-41-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for HIV-1 inhibitors)
IT 121-45-9, Trimethyl phosphite 139964-36-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of HIV-a inhibitors)
IT 84337-41-7D, halo deriv.
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with tri-Me phosphite)

L17 ANSWER 37 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 116:84108 MARPAT
TITLE: Preparation of (3'-azido-2',3'-dideoxy) purine nucleosides as medical antivirals
INVENTOR(S): Rideout, Janet Litster; Freeman, George Andrew; Short, Steven Andersen; Almond, Merrick Richard; Collins, Jon Loren
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 45 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 421739	A1	19910410	EP 1990-310788	19901002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DD 299188	A5	19920402	DD 1990-344335	19901001
CA 2026730	AA	19910404	CA 1990-2026730	19901002
AU 9063716	A1	19910411	AU 1990-63716	19901002
AU 632369	B2	19921224		
CN 1051180	A	19910508	CN 1990-108846	19901002
CN 1027373	B	19950111		
HU 55407	A2	19910528	HU 1990-6302	19901002
HU 208702	B	19931228		

JP 03167197	A2	19910719	JP 1990-264928	19901002
ZA 9007877	A	19920624	ZA 1990-7877	19901002
US 5153318	A	19921006	US 1990-591916	19901002
PRIORITY APPLN. INFO.:			GB 1989-22285	19891003
			GB 1990-16775	19900731

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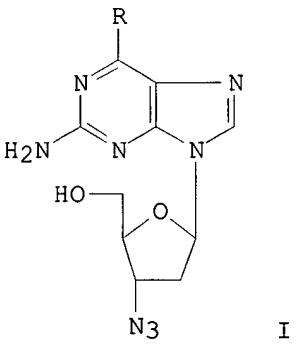

I

AB 3'-Azido-2',3'-dideoxy purine nucleosides I [R = halo, C1-6 alkoxy, C3-6 cycloalkoxy, (substituted) aryloxy, (substituted) amino, 1-azetidinyl, 1-pyrrolidinyl, etc.], useful for treatment of infection by HIV and hepatitis B viruses, were prepd. Thus, 2-amino-9-[3-O-mesyl-5-O-(methoxycarbonyl)-.beta.-D-xylofuranosyl]-6-methoxy-9H-purine (prepn. given) was subjected to 1) condensation with ClC(S)OPh 2) removal of the resulting thiobenzoate by redn. with n-Bu3SnH/AIBN in PhMe, 3) reaction with NaN3, and 4) deprotection by NaOMe/MeOH to give title compd. I (R = OMe) (II). The IC50's for II against HIV-1 and HIV-2 in MT4 cells were 5.6 .mu.M and 5.5 .mu.M, resp. Formulations of I were prepd.

IC ICM C07H019-173
ICS A61K031-70

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 16, 63

ST azidodideoxypurine nucleoside prepn antiviral; HIV inhibitor azidodideoxypurine nucleoside; hepatitis B treatment azidodideoxypurine nucleoside; transglycosidation enzymic purine deoxythymidine; glycosidation trans enzymic purine deoxythymidine

IT Virucides and Virustats
((azidodideoxypentofuranosyl)purine nucleosides)

IT Nucleosides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(3'-azido-2',3'-dideoxyribo-, purine, prepn. of, as medical antivirals)

IT Virus, animal
(hepatitis B, infection with, treatment of, (azidodideoxypentofuranosyl)purine nucleosides for)

IT Virus, animal
(human immunodeficiency 1, inhibitors, azidodideoxyribo purine nucleosides)

IT Virus, animal
(human immunodeficiency 2, inhibitors, azidodideoxyribo purine nucleosides)

IT Virus, animal

(retro-, inhibitors, azidodideoxyribo purine nucleosides)

IT Glycosidation
(trans-, enzymic, in prepn. of medical antivirals)

IT 5437-49-0, 2-Amino-6-dimethylaminopurine 6331-91-5 18202-53-4 19916-73-5, 2-Amino-6-benzyloxypurine 20535-83-5, 2-Amino-6-methoxypurine 51866-19-4, 2-Amino-6-ethoxypurine 76412-62-9 134760-64-8 134760-65-9 134760-66-0 134760-67-1 134760-68-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with azidodeoxythymidine, in presence of transferase enzyme)

IT 9026-93-1, Adenosine deaminase
RL: RCT (Reactant); RACT (Reactant or reagent)
(deamination by, of purine deriv., in prepn. of medical antivirals)

IT 134760-70-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and condensation of, with azidodeoxythymidine, in prepn. of medical antivirals)

IT 3056-33-5P 9026-86-2P, trans-N-Deoxyribolase 57024-70-1P 66323-46-4P 134760-57-9P 134760-58-0P 134760-59-1P 134760-60-4P 134760-61-5P 134760-62-6P 134760-63-7P 134760-69-3P 134760-76-2P 134760-77-3P 134782-54-0P 138676-13-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in prepn. of medical antivirals)

IT 5432-33-7P 134760-73-9P 134760-74-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as antiviral)

IT 55146-05-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for antivirals)

IT 134760-40-0P 134760-41-1P 134760-42-2P 134760-43-3P 134760-44-4P 134760-45-5P 134760-46-6P 134760-47-7P 134760-48-8P 134760-49-9P 134760-50-2P 134760-51-3P 134760-52-4P 134760-53-5P 134760-54-6P 134760-55-7P 134760-56-8P 134760-71-7P 134760-72-8P 134760-74-0P 134782-53-9P 135909-45-4P 138676-14-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as medical antiviral agent)

IT 64-04-0, Phenethylamine 64-17-5, Ethanol, reactions 67-56-1, Methanol, reactions 67-63-0, Isopropanol, reactions 71-23-8, Propanol, reactions 71-36-3, n-Butanol, reactions 73-40-5, Guanine 74-89-5, Methylamine, reactions 75-04-7, Ethylamine, reactions 79-22-1, Methyl chloroformate 83-01-2, Diphenylcarbamyl chloride 95-62-5 100-51-6, Benzyl alcohol, reactions 107-10-8, Propylamine, reactions 108-24-7, Acetic anhydride 108-95-2, Phenol, reactions 109-73-9, n-Butylamine, reactions 123-75-1, Pyrrolidine, reactions 124-40-3, Dimethylamine, reactions 124-63-0, Methanesulfonyl chloride 503-29-7, Azetidine 624-78-2 627-35-0, N-Methylpropylamine 765-30-0, Cyclopropylamine 1005-56-7 2251-65-2 2516-34-9, Cyclobutylamine 2919-23-5, Cyclobutanol 5163-20-2, N-Methylcyclopropylamine 10025-87-3, Phosphorus oxychloride 10310-21-1, 2-Amino-6-chloropurine 19597-69-4, Lithium azide

30516-87-1 32605-52-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of medical antivirals)

L17 ANSWER 38 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 116:37531 MARPAT
TITLE: Reversible modification of biological compounds for detection, separation and purification thereof
INVENTOR(S): Coull, James M.; Gildea, Brian; Koester, Hubert
PATENT ASSIGNEE(S): Millipore Corp., USA
SOURCE: Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 424819	A1	19910502	EP 1990-120093	19901019
EP 424819	B1	19941228		
R: DE, FR, GB, IT, NL, SE				
US 5410068	A	19950425	US 1989-425740	19891023
JP 03279371	A2	19911210	JP 1990-283585	19901023
PRIORITY APPLN. INFO.:			US 1989-425740	19891023

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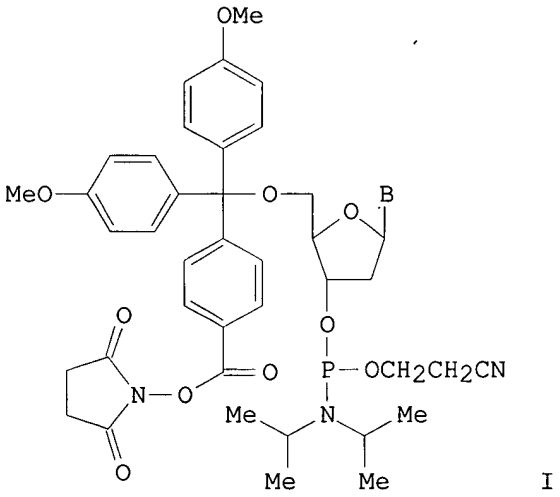

I

AB Compds. and methods are provided for the reversible modification of natural products, natural product synthons, biopolymers, or biopolymer synthons, e.g. nucleosides, nucleotides, oligonucleosides. The modification allows a variety of chemistries to be performed on these compds., yet can be removed to regenerate functional groups on the natural product, biopolymer, or synthon of

interest. The compds. of the invention serve as a protecting group for a functional group on the natural product, biopolymer, or synthon, and as a linking group for attaching a modifying moiety thereto. Prepn. of N-succinimidyl-4-[bis-4-(methoxyphenyl)-5'-O-(3'-O-(N,N-diisopropylamino-2-cyanoethylphosphinyl)-2-deoxynucleosidyl)-methyl] benzoates (I), e.g. I (B = thymine), is described. The modified nucleosides were used in the synthesis of biotin- and fluorescein-labeled polymerase chain reaction (PCR) oligonucleotide primers. Use of the 5'-modified oligonucleotides of the invention for the purifn. of PCR products was demonstrated.

IC ICM C07H021-00
ICS C12Q001-68; C07C015-16

CC 9-14 (Biochemical Methods)
Section cross-reference(s): 3, 33

ST biopolymer heterofunctional protecting group prepn; natural product heterofunctional protecting group; synthon heterofunctional protecting group; oligonucleotide protecting group polymerase chain reaction

IT Fluorescent substances
Luminescent substances
(conjugates with heterofunctional protecting group for biopolymer or natural product or synthon)

IT Synthons
Alkaloids, biological studies
Amino acids, biological studies
Biopolymers
Carbohydrates and Sugars, biological studies
Lipids, biological studies
Monosaccharides
Natural products
Nucleic acids
Nucleosides, biological studies
Nucleotides, biological studies
Oligosaccharides
Peptides, biological studies
Proteins, biological studies
Steroids, biological studies
RL: BIOL (Biological study)
(heterofunctional protecting groups for)

IT Protective groups
(heterofunctional, for biopolymers and natural products and synthons)

IT Deoxyribonucleic acids
RL: ANST (Analytical study)
(of .lambda. bacteriophage, polymerase chain reaction oligonucleotide primer for, with heterofunctional protecting group)

IT Luminescent substances
(chemi-, conjugates with heterofunctional protecting group for biopolymer or natural product or synthon)

IT Polymers, compounds
Radioelements, compounds
RL: ANST (Analytical study)
(conjugates, with heterofunctional protecting group for biopolymer or natural product or synthon)

IT Virus, bacterial
(lambda, DNA of, polymerase chain reaction oligonucleotide primer for, with heterofunctional protecting group)

IT Nucleotides, polymers
RL: BIOL (Biological study)
(oligo-, heterofunctional protecting groups for)
IT 60-32-2 373-44-4, 1,8-Diaminooctane 534-03-2, 2-Amino-1,3-propanediol 616-30-8, 3-Amino-1,2-propanediol 2783-17-7, 1,12-Dodecanediamine 4048-33-3, 6-Aminohexanol
RL: ANST (Analytical study)
(aminolysis of hydroxysuccinimidyl group of heterofunctional protecting group-contg. nucleoside deriv. with)
IT 108-91-8, Cyclohexylamine, reactions 109-76-2, 1,3-Diaminopropane 110-60-1, 1,4-Diaminobutane 111-26-2, 1-Hexanamine 124-09-4, 1,6-Diaminohexane, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(aminolysis of hydroxysuccinimidyl group of heterofunctional protecting group-contg. nucleoside deriv. with)
IT 58-85-5D, Biotin, conjugates with heterofunctional linking groups
RL: ANST (Analytical study)
(for biopolymers and natural products and synthons)
IT 111-86-4, 1-Octanamine 124-22-1, 1-Dodecanamine 124-30-1, 1-Octadecanamine 2016-57-1, 1-Decanamine 2570-26-5, 1-Pentadecanamine
RL: ANST (Analytical study)
(heterofunctional protecting group-contg. oligonucleotide reaction with)
IT 107-10-8, 1-Propanamine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(heterofunctional protecting group-contg. oligonucleotide reaction with)
IT 132454-42-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, for polymerase chain reaction primer prepn., amplified nucleic acid isolation in relation to)
IT 132454-38-7P 132454-39-8P 132454-40-1P 132454-41-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in prepn. of heterofunctional protecting group for nucleoside deriv.)
IT 138158-85-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of and aminolysis of)
IT 35013-72-0DP, N-Hydroxysuccinimidyl biotin, reaction products with heterofunctional protecting group-contg. nucleoside deriv. 138251-25-9DP, reaction products with heterofunctional protecting group-contg. nucleoside deriv.
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for polymerase chain reaction primer)
IT 132454-46-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for polymerase chain reaction primer prepn., amplified nucleic acid isolation in relation to)
IT 90-96-0, 4,4'-Dimethoxybenzophenone 6066-82-6, N-Hydroxysuccinimide 32664-14-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of heterofunctional protecting group for nucleoside deriv.)
IT 138159-79-2D, heterofunctional protecting group-contg. nucleoside

deriv.-contg.
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with aminodecane, multiplex oligonucleotide purifn. in relation to)
IT 138159-47-4D, heterofunctional protecting group-contg. nucleoside deriv.-contg.
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with aminohexane, multiplex oligonucleotide purifn. in relation to)
IT 138159-53-2D, heterofunctional protecting group-contg. nucleoside deriv.-contg. 138159-54-3D, heterofunctional protecting group-contg. nucleoside deriv.-contg.
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with biotin or fluorescein label, for polymerase chain reaction oligonucleotide primer)

L17 ANSWER 39 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 115:72155 MARPAT
TITLE: Nucleoside and polynucleotide thiophosphoramidite and phosphorodithioate compounds and processes
INVENTOR(S): Caruthers, Marvin H.; Brill, Wolfgang; Nielsen, John; Yau, Eric; Ma, Yun Xi
PATENT ASSIGNEE(S): University Patents, Inc., USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9104983	A1	19910418	WO 1990-US5653	19901004
W: AU, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
AU 9066036	A1	19910428	AU 1990-66036	19901004
PRIORITY APPLN. INFO.:			US 1989-417387	19891005
			US 1990-488805	19900303
			WO 1990-US5653	19901004

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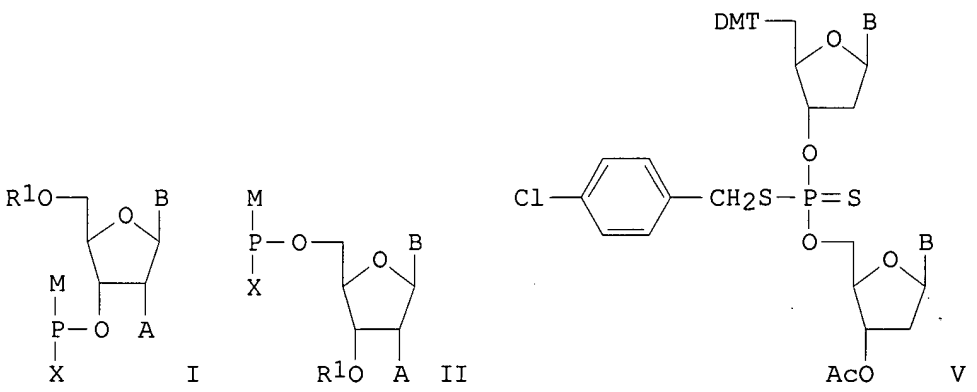


AB Nucleoside thiophosphoramidites [I or II; B = (deoxy)nucleoside base; A = H, OH, halo, SH, NH2, N3, OR2, SR2, NHR2; R2 = heteroatom-(un)substituted blocking group; R1 = blocking group; M = SR5; X = NR6R7; R5-R7 = heteroatom-(un)substituted (cyclo)alkyl, aryl, aralkyl, cycloalkylalkyl, (cyclo)alkenyl, aralkenyl, (cyclo)alkynyl, aralkynyl; R6R7 = C.ltoreq.5 alkylene; NR6R7 = N-heterocyclyl contg. .gtoreq.1 addnl. heteroatom selected from N, O, and S], useful for synthesizing mononucleotides and polynucleotides having phosphorodithioate, phosphorothioamidate, phosphorothiotriester, and phosphorothioate internucleotide linkages, are prepd. Thus, 2.5 mol (Me2CH)2NH was added slowly to a vigorously stirred and cooled (-18.degree.) soln. of 0.5 mol PCl3 in THF and the reaction mixt. refluxed for 12 h and, after removing (Me2CH)2NH.HCl, for addnl. 12 h to give, after crystn. from hexane, [(Me2CH)2N]2PCl (III), as a colorless cryst. solid. p-ClC6H4CH2SH (50 mmol) was treated with 50 mmol NaH in Et2O with stirring and after 2 h 50 mmol III was added and the reaction mixt. stirred at room temp. for 4 h to give, after recrystn. from MeCN, p-ClC6H4CH2SP[N(CHMe2)2]2 (IV). To a suspension of 5 mmol 5'-O-(di-p-anisylphenylmethyl)thymidine and 6 mmol IV in MeCN was added 10 mmol tetrazole and the reaction mixt. was stirred at room temp. for 16 h to give 80.1% I [B = 1-thyminyl, A = H, R1 = di-p-anisylphenylmethyl (DMT), M = SCH2C6H4Cl-p, X = N(CHMe2)2]. This (0.2 mmol) was coupled with 3'-O-acetylthymidine in DMF contg. nitrophenyltetrazole and, after 15 min, quenched with 1 mmol S to give dinucleotide phosphorodithioate (V).

IC ICM C07H021-00
ICS C07H021-04; C07F009-02

CC 33-10 (Carbohydrates)

ST nucleoside thiophosphoramidite phosphorodithioate prepn; polynucleotide thiophosphoramidite phosphorodithioate; phosphorothioamidate nucleoside polynucleotide; phosphorothiotriester nucleoside polynucleotide

IT Nucleotides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(thiophosphoramidites and phosphorodithioates, prepn. of, as intermediates for polynucleotides having phosphorodithioate and/or phosphorothioate and/or phosphorothioamidate internucleotide linkages)

IT Nucleotides, polymers

RL: RCT (Reactant); RACT (Reactant or reagent)
(poly-, phosphorodithioates and/or phosphorothioates and/or phosphorothioamidates, intermediates for, nucleoside thiophosphoramidites and phosphorodithioates as)

IT 108-18-9, Diisopropylamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(amination by, of phosphorus trichloride)

IT 7719-12-2, Phosphorus trichloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(amination of, by diisopropylamine)

IT 40615-39-2 64325-78-6 67219-55-0 68892-41-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with (chlorobenzylthio)bis(diisopropylamino)phosphine)

IT 65978-10-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with (cyanomethyl)tetraisopropylphosphorodiamidite)

IT 102691-36-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with adenosine deriv.)

IT 6258-66-8, p-Chlorobenzyl mercaptan
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with bis(diisopropylamino)chlorophosphine)

IT 56183-63-2, Bis(diisopropylamino)chlorophosphine 98796-51-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with chlorobenzyl mercaptan)

IT 102691-36-1, Bis(diisopropylamino)-2-cyanoethoxyphosphine
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with dinucleoside phosphorodithioate triester)

IT 21090-30-2, 3'-O-Acetylthymidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with nucleoside thiophosphoramidites)

IT 613-13-8, 2-Aminoanthracene
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with thymidine hydrogenphosphonodithioate)

IT 288-88-0, 1H-1,2,4-Triazole
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with trichlorophosphine)

IT 1468-95-7, 9-Anthracenemethanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxidative condensation of, with dinucleoside hydrogenphosphonothioate)

IT 120047-01-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and condensation of, with nucleoside derivs.)

IT 134645-83-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and condensation of, with thymidine deriv.)

IT 118149-24-9P 118149-25-0P 118149-27-2P 118149-28-3P
118149-29-4P 118149-30-7P 118149-31-8P 120047-02-1P
120047-04-3P 120047-05-4P 120047-06-5P 120065-31-8P
124667-71-6P 126866-95-3P 126866-97-5P 128981-12-4P
128981-13-5P 129624-19-7P 129624-21-1P 129624-23-3P
129789-66-8P 132928-34-8P 132928-35-9P 135098-93-0P
135098-94-1P 135098-95-2P 135098-96-3P 135098-97-4P
135098-98-5P 135098-99-6P 135099-00-2P 135099-01-3P
135099-02-4P 135099-03-5P 135099-04-6P 135099-05-7P

135099-06-8P 135099-07-9P 135099-08-0P 135099-09-1P
135099-10-4P 135099-11-5P 135099-12-6P 135099-13-7P
135099-14-8P 135099-15-9P 135099-16-0P 135099-18-2P
135099-19-3P 135099-20-6P 135099-21-7P 135099-22-8P
135099-23-9P 135099-24-0P 135099-25-1P 135099-26-2P
135099-27-3P 135099-28-4P 135099-29-5P 135099-30-8P
135099-31-9P 135099-32-0P 135129-25-8P 135129-26-9P
135129-27-0P 135213-68-2P 135213-69-3P 135213-70-6P
135213-71-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for polynucleotides having phosphorodithioate and/or phosphorothioate and/or phosphorothioamidate internucleotide linkages)

IT 135116-60-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, nucleoside thiophosphoramidites and phosphorodithioates as intermediates for)

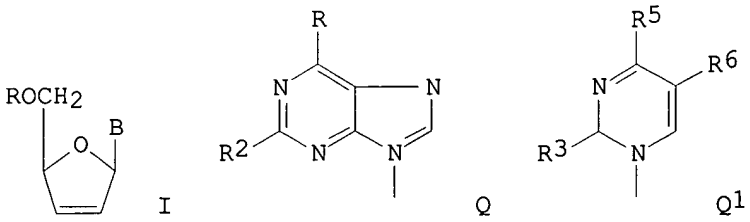
IT 115147-72-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(sulfuration of, by hydrogen sulfide)

IT 98796-51-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(sulfuration of, with hydrogen sulfide)

L17 ANSWER 40 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 112:179714 MARPAT
TITLE: Preparation of 2',3'-didehydro-1',3'-dideoxy nucleosides as antivial prodrugs
INVENTOR(S): Starrett, John E., Jr.; Mansuri, Muzammil M.; Martin, John C.
PATENT ASSIGNEE(S): Bristol-Myers Co., USA
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 340778	A2	19891108	EP 1989-108099	19890505
EP 340778	A3	19901122		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 02152976	A2	19900612	JP 1989-112371	19890502
FI 8902132	A	19891107	FI 1989-2132	19890503
NO 8901835	A	19891107	NO 1989-1835	19890503
DK 8902217	A	19891107	DK 1989-2217	19890505
AU 8934071	A1	19891109	AU 1989-34071	19890505
ZA 8903348	A	19900131	ZA 1989-3348	19890505
PRIORITY APPLN. INFO.:			US 1988-190809	19880506
			US 1989-333449	19890407

GI



I Q Q1

AB The title compds. [I; R = H, alkanoyl, cycloalkanoyl, alkenoyl, etc.; B = Q, Q1; R1, R2 = H, OH, F, Cl, Br, NH2, etc.; R3 = OH, NH2, HS; R5 = H, OH, HS, NH2; R6 = H, alkyl, alkenyl, etc.], useful as antiviral prodrugs particularly active against HIV, are prepd. 2',3'-Didehydro-2',3'-dideoxythymidine was acetylated with AcCl in pyridine to give 5'-O-acetyl-2',3'-didehydro-2',3'-dideoxythymidine (II). In an in vitro study II had an ID50 of 3.2 .mu.M against HIV (LAV strain) vs. 0.2 .mu.M for 2',3'-didehydro-2',3'-dideoxythymidine.

IC ICM C07D473-00
ICS C07D405-04; C07D405-14; A61K031-505; A61K031-52

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1

ST didehydrodideoxy nucleoside prepn antiviral; prodrug antiviral didehydrodideoxy nucleoside; HIV infection treatment didehydrodideoxy nucleoside

IT Virucides and Virustats
(didehydrodideoxynucleosides)

IT Immunodeficiency
(acquired immune deficiency syndrome, treatment of, dehydrodideoxynucleosides for)

IT Virus, animal
(human immunodeficiency, inhibitors, didehydrodideoxynucleosides)

IT Pharmaceutical dosage forms
(prodrugs, didehydrodideoxynucleosides, antiviral)

IT 6038-56-8P 77421-68-2P 118869-95-7P 122567-97-9P 122567-98-0P 122567-99-1P 126209-26-5P 126209-27-6P 126209-28-7P 126209-29-8P 126209-30-1P 126209-31-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antiviral prodrug)

IT 67-56-1, Methanol, reactions 74-88-4, Methyl iodide, reactions 98-88-4, Benzoyl chloride 108-93-0, Cyclohexanol, reactions 530-62-1, Carbonyl diimidazole 3056-17-5 3282-30-2, Pivaloyl chloride 5974-93-6, 2',3'-Didehydro-2',3'-dideoxyuridine 20260-53-1, Nicotinyl chloride hydrochloride 38870-89-2, Methoxyacetyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of didehydrodideoxynucleosides as antiviral prodrugs)

L17 ANSWER 41 OF 44 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 112:119355 MARPAT
TITLE: Preparation of 2',3'-dideoxy-2',3'-didehydro-pyrimidine,-azapyrimidine, or -deazapyrimidine nucleosides as antiviral agents against human immunodeficiency viruses (HIV)

INVENTOR(S): Starrett, John E., Jr.; Mansuri, Muzammil M.; Martin, John C.; Fuller, Carl E.; Howell, Henry G.
PATENT ASSIGNEE(S): Bristol-Myers Co., USA
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 334368	A2	19890927	EP 1989-105269	19890323
EP 334368	A3	19911227		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 4904770	A	19900227	US 1988-173473	19880324
NO 8901208	A	19890925	NO 1989-1208	19890320
NO 171367	B	19921123		
FI 8901338	A	19890925	FI 1989-1338	19890321
FI 93111	B	19941115		
FI 93111	C	19950227		
IL 105572	A1	19940412	IL 1989-105572	19890321
IL 105573	A1	19940412	IL 1989-105573	19890321
IL 105571	A1	19940530	IL 1989-105571	19890321
IL 89693	A1	19940826	IL 1989-89693	19890321
IL 105570	A1	19940826	IL 1989-105570	19890321
DK 8901464	A	19890925	DK 1989-1464	19890322
ZA 8902166	A	19920226	ZA 1989-2166	19890322
AU 8931673	A1	19890928	AU 1989-31673	19890323
AU 622439	B2	19920409		
JP 02149595	A2	19900608	JP 1989-71592	19890323
US 5130421	A	19920714	US 1991-697512	19910429
NO 9103456	A	19890925	NO 1991-3456	19910903
NO 172345	B	19930329		
NO 172345	C	19930707		
NO 9103457	A	19890925	NO 1991-3457	19910903
NO 171314	B	19921116		
NO 171314	C	19930224		
NO 9103458	A	19890925	NO 1991-3458	19910903
NO 171315	B	19921116		
NO 171315	C	19930224		
NO 9103459	A	19890925	NO 1991-3459	19910903
NO 171316	B	19921116		
NO 171316	C	19930224		
US 5212294	A	19930518	US 1992-860938	19920331
FI 9405698	A	19941202	FI 1994-5698	19941202
FI 9405699	A	19941202	FI 1994-5699	19941202
FI 9405700	A	19941202	FI 1994-5700	19941202
CA 1339483	A1	19970930	CA 1996-617047	19960321
PRIORITY APPLN. INFO.:			US 1988-173473	19880324
			CA 1989-593738	19890315
			NO 1989-1208	19890320
			IL 1989-89693	19890321
			US 1989-441023	19891124
			US 1991-697512	19910429
			FI 1994-103	19940110

OTHER SOURCE(S): CASREACT 112:119355